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# DISEASES *of the* CHEST

OFFICIAL PUBLICATION



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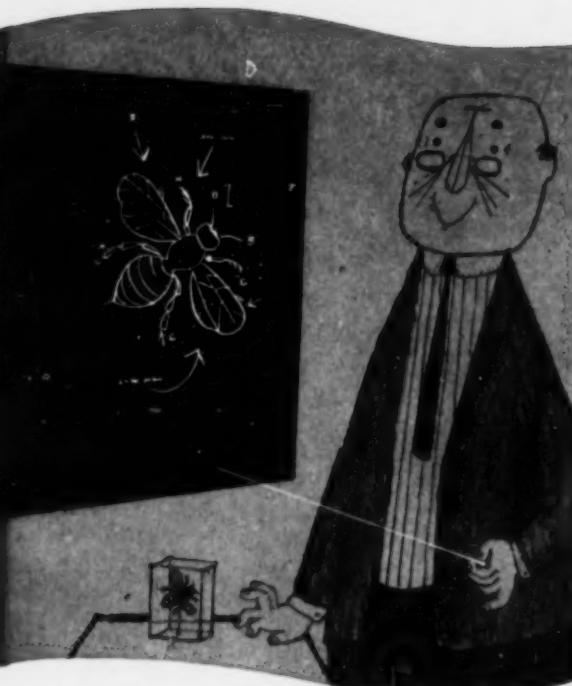
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**Third International Congress on Diseases of the Chest**  
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# chronic asthmatic

... back  
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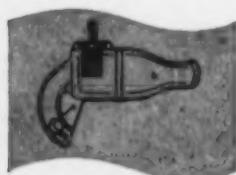
1. Kaufman, R., and Farmer, L. (1951) Norisodrine by Aerohalor in Asthma, *Ann. Allergy*, 9:89, Jan.-Feb.
2. Swartz, H. (1950) Norisodrine Sulfate (25 Per Cent) Dust Inhalation in Severe Asthma, *Ann. Allergy*, 8:488, July-August.
3. Kropp, L., Grossman, M., and Ivy, A. (1949) The Inhalation of 1-[3',4'-Dihydroxyphenyl]-2-isopropylbenzene (Norisodrine Sulfate Dust), *J. Allergy*, 20:111, March.

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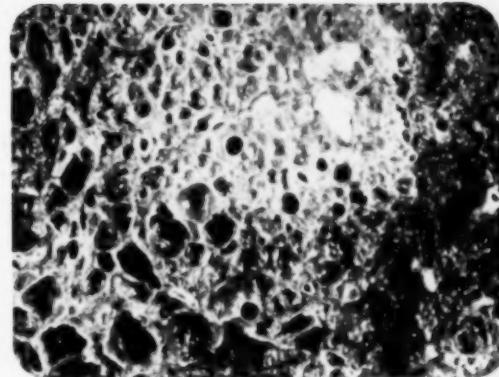
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1. Herk, W. C.: Reduced Otoxicity by Combined Streptomycin-Dihydrostreptomycin Treatment of Tuberculosis, Scientific Exhibit 317, 102nd Annual Meeting A.M.A., New York, June 1-5, 1953.

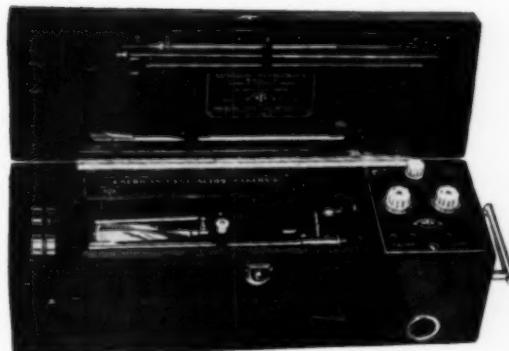


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I. Boger, et al.: Oral Penicillin: Evaluation of All Forms, report distributed at New York Session of the A.M.A., 1953.

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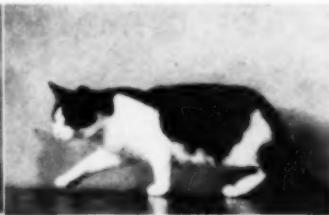
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1. Hobby, G. L., Lenert, T. F., Rivoire, Z. C., Donikian, M., and Pikula, D.: Am. Rev. Tuberc. 67:808, 1953.

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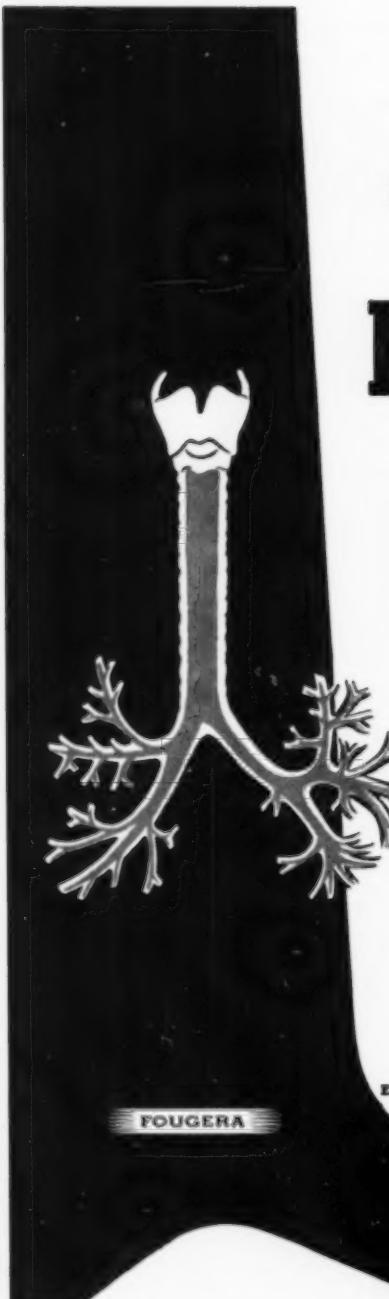
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1. Meakins, J. C.: *The Practice of Medicine*, ed. 5, St. Louis, The C. V. Mosby Company, 1950, p. 154.

2. *Ibid.*, p. 268.

3. Bishop, P. A., and Lindsley, G. E.: *Lung Abscess*, in Fillmore, G. U.: *Clinical Radiology*, Philadelphia, F. A. Davis Company, 1950, vol. 1, p. 339.

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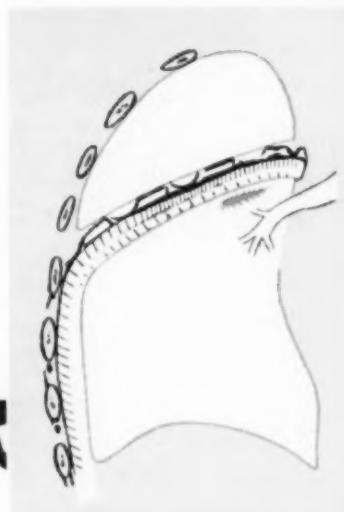
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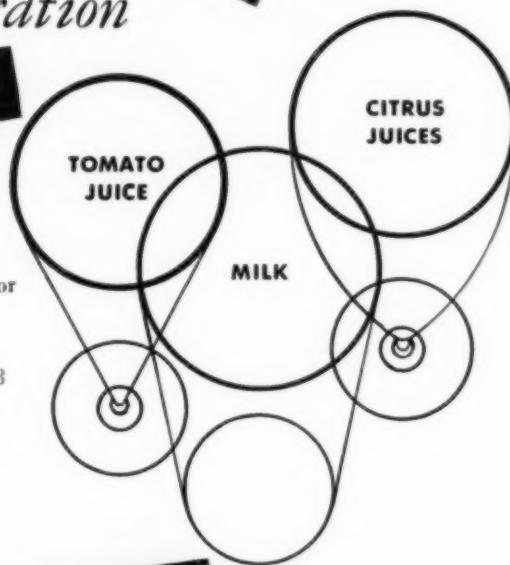
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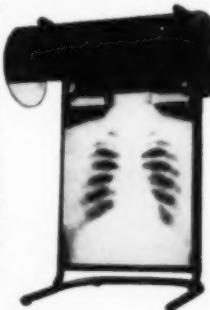


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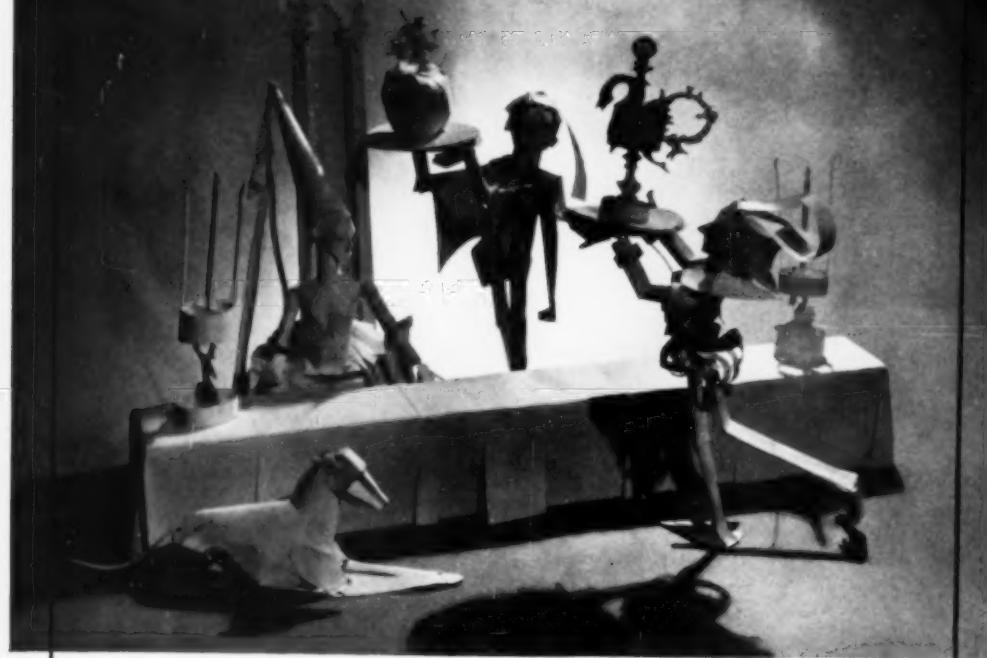
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# DISEASES of the CHEST

VOLUME XXIV

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NUMBER 6

## Clinical Observations on Viomycin Sulphate in the Treatment of Tuberculosis\*

ROBERT L. HACKNEY, M.D., ERNEST Q. KING, M.D.,  
EDWARD E. MARSHALL, D.Sc., K. ALBERT HARDEN, M.D.  
and HOWARD M. PAYNE, M.D.

Washington, D. C.

Viomycin,\*\* a new antituberculous agent was isolated independently by Findlay et al.<sup>1</sup> and Bartz and his co-workers<sup>2</sup> from two actinomycete believed to be new strains of streptomycetes. *Streptomyces puniceus* and *Streptomyces floridae* have been proposed as the names of these new strains. The two new strains have not been proven identical, but probably are.

Numerous investigators including the original workers, Hobby, et al.<sup>3</sup> Steenken and Wolinsky,<sup>4</sup> and Youmans and Youmans,<sup>5</sup> reported that in vitro, viomycin had inhibitory activity against *Mycobacterium tuberculosis*. It was found to be effective against streptomycin sensitive and streptomycin resistant organisms in experimental tuberculosis in animals.

The drug was described at the Ninth Streptomycin Conference of the Veteran's Administration<sup>6</sup> in April, 1950. Following this announcement five patients with far advanced pulmonary tuberculosis and without history of previous antimicrobial therapy were treated with this drug. The purpose of these early studies was to determine the antimicrobial efficacy and the chronic toxicity of Viomycin.

These patients received 3 grams of viomycin daily for 13 weeks. In Table I, it can be seen that proteinuria developed early in treatment in all five patients. Despite the evidence of small losses of urine albumin in qualitative determinations (Table I), quantitative determination revealed that from 7.2 to 26.2 grams of protein per liter was lost. Urea clearance tests showed a diminished rate of clearance for all patients in the third month (Table II). One patient developed uremia during the last three weeks of treatment and died four weeks after the drug was discontinued. This patient also had hypokalemia just prior to the onset of uremia. The urea clearance tests of four patients showed gradual improvement with discontinuance

\*From the Division of Chronic Chest Diseases of Freedmen's Hospital and Howard University.

This work was supported in part by a grant from the Shrine Tuberculosis and Cancer Foundation.

\*\*Furnished by Dr. Gladys Hobby, Chas. Pfizer & Company, Inc.

TABLE I  
SPECIFIC GRAVITY AND ALBUMIN REPORTED IN A.M.  
URINE EXAMINATIONS OF FIVE PATIENTS TREATED WITH VIOMYCIN  
SULPHATE 3G DAILY FOR 13 WEEKS BY WEEKS OF OBSERVATION

Patient	Observation Week	2nd Week	4th Week	6th Week	8th Week	10th Week	12th Week	17th Week	21st Week	42nd Week
A	1.025 Neg.	1.018 2 +	1.011 2 +	1.010 2 +	1.015 1 +	1.012 2 +	1.010 2 +	1.010 Neg.	1.010 Trace	Died 19th Wk.
B	1.018 Neg.	1.018 Trace	1.012 2 +	1.012 2 +	1.010 1 +	1.010 1 +	1.010 2 +	1.010 Neg.	1.010 Trace	1.011* 2 +
C	1.022 Neg.	1.022 Neg.	1.023 Trace	1.014 1 +	1.020 1 +	1.016 Trace	1.016 2 +	1.027 Neg.	1.027 Neg.	1.018 Neg.
D	1.024 Neg.	1.010 Neg.	1.015 Trace	1.010 1 +	1.016 1 +	1.010 2 +	1.005 1 +	1.015 Neg.	1.015 Trace	1.010 Neg.
E	1.014 Neg.	1.013 Neg.	1.013 1 +	1.009 2 +	1.012 2 +	1.010 1 +	1.009 1 +	1.008 Neg.	1.008 Trace	1.007 Trace

\*Patient "B" died in the 30th week of observation.

of viomycin. Loss of protein in the urine ceased and no evidences of permanent renal damage occurred.

Figure 1 reveals that viomycin sulfate, 3 grams daily, caused a return of the temperature to normal in all patients, but a return of fever as soon as the drug was discontinued in four out of five patients. In Figure 2 it can be noted that after improvement in the chest roentgenograms during the first two months, spread occurred later during treatment in all but one patient.

On the basis of these studies it was concluded that 3 grams of viomycin sulfate daily had a definite antimicrobial effect, but was too toxic for widespread use in tuberculosis therapy.

Shortly after these studies Tempel<sup>7</sup> reported that viomycin sulfate, 2 grams every three days, could be administered safely to patients in combination with PAS or streptomycin. On the basis of this report it was determined that a group of patients should have viomycin, 2 grams twice

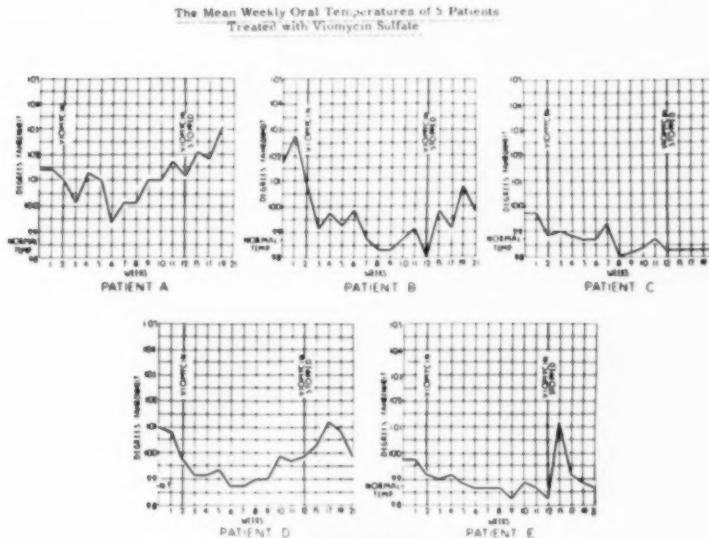


FIGURE 1

TABLE II: THE RESULTS OF UREA CLEARANCE TESTS IN FIVE PATIENTS RECEIVING 3 GRAMS OF VIOMYCIN DAILY FOR 13 WEEKS

Patient	12th Week Per cent	17th Week Per cent	23rd Week Per cent
A	12.5	7.1	Died
B	36	20	96
C	30	33	98.5
D	18.34	20.61	88
E	17.5	20.45	90.5

weekly and comparable patients should have dihydrostreptomycin in 2 gram twice weekly dosages and that both groups should have sodium PAS, 12 grams daily.

#### *The Group Studied*

Patients were matched roughly for equivalent types of disease and duration of illness. They ranged from 16 to 53 years of age. No diabetics and none with evidence of renal impairment were included in either group. None of these patients showed severe metabolic deterioration as a result of tuberculosis.

The group reported consists of 35 patients treated with viomycin and PAS. Seven of them had organisms resistant to 100 mcg. of streptomycin prior to selection for treatment. Four were ambulatory.

The control group consisted of 24 treated with streptomycin and PAS. One with no history of previous streptomycin treatment was reported to have organisms resistant to 100 mcg. of streptomycin shortly after treatment.

These patients were treated by whatever other methods which were applicable.

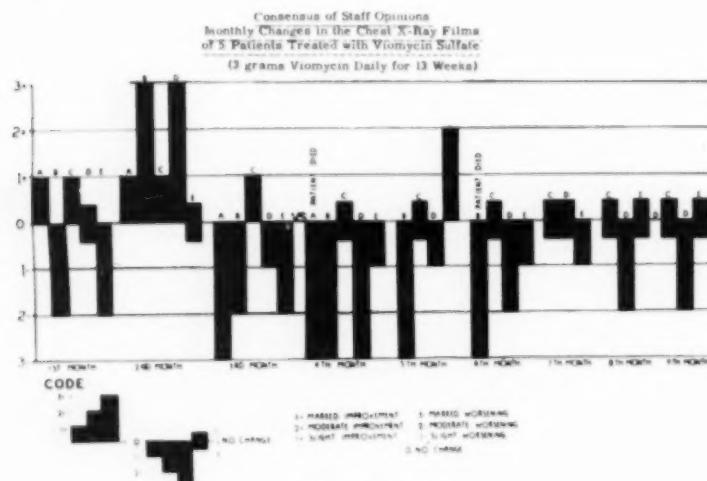


FIGURE 2

TABLE III: THE DURATION OF OBSERVATION OF 59 PATIENTS TREATED WITH 2 GRAMS OF VIOMYCIN OR STREPTOMYCIN TWICE WEEKLY AND 12 GRAMS OF SODIUM PAS DAILY

Regimen	No. of Patients	MONTHS OF OBSERVATION					
		1	2	3	4	5	6
Viomycin-PAS	35	0	0	1	5	3	26
Streptomycin-PAS	24	0	1	0	9	0	14

### Evidences of Toxicity

**Signs of Local Toxicity:** Both viomycin sulfate and dihydrostreptomycin were dissolved in proportions of 1 gram to each 2 cc. of distilled water and given intramuscularly, 1 gram in each gluteal muscle twice weekly. Viomycin injected in this dilution caused no unusual complaints of discomfort or local reaction. Minor complaints of local soreness were equally common among both groups.

**Auditory and Vestibular Damage:** After five to six months of treatment, audiograms revealed diminished hearing in six of 23 viomycin treated patients. Three with abnormal audiograms had history of previous streptomycin treatment. The other three had losses of 30 to 60 decibels at 1,024 cycles and above.

Evidence of damage to the vestibular branch of the eighth nerve was shown by loss of response to caloric stimulation in three of 10 patients treated with viomycin. Two of them were known to have received previous

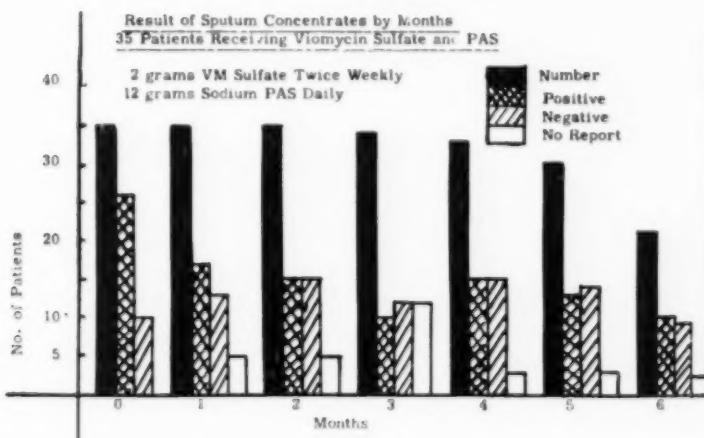
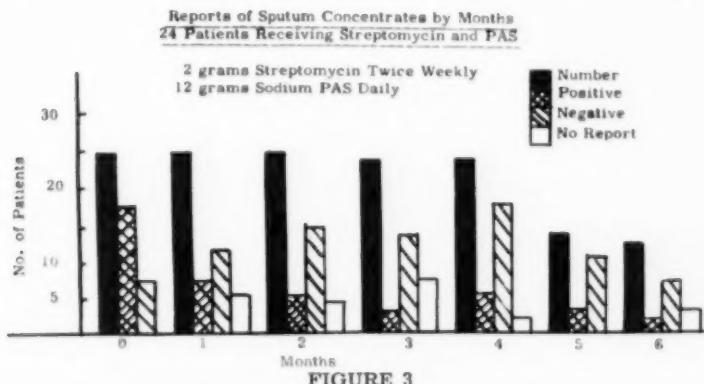


TABLE IV  
THE RESPONSE TO VIOMYCIN OF SEVEN PATIENTS RESISTANT TO STREPTOMYCIN  
Two grams Viomycin Sulfate Twice Weekly, 12 grams Sodium PAS Daily

Patient	Initial Temperature	Temperature After One Month	Tendency Before Viomycin Therapy	Viomycin Weight	Weight After Two Months Viomycin Therapy	X-RAY CHANGES BY MONTHS					
						Before Viomycin Therapy	1	3	5	6	Proposis
A.T.	100	98.6	L	165	157	W	I	I	S	Improved	
L.G.	98.6	98.6	S	89	91	W	S	S	I	S	Improved
J.A.	98.6	98.6	S	81	88	W	I	S	I	S	Improved
E.L.	98.6	98.6	S	116	117	S	S	S	S	S	Improved (to surgery)
D.L.	98.6	98.6	S	91	98	W	I	W	S	S	Improved
A.R.	100	98.6	S	92	99	W	I	S	S	W	Improved
S.S.	100	98.6	S	120	123	W	S	S	S	I	Improved

Code: W = Worse  
S = Stable  
I = Improved  
L = Losing

courses of streptomycin. In the streptomycin treated group nine of 26 tests were positive. Seven of these had no previous streptomycin treatment.

**Renal Toxicity:** In neither group have we observed abnormalities in the urine specific gravity, non protein nitrogen, plasma proteins, or electrolyte balance. No tendency to excrete protein in the urine has been observed. Although reports of a trace of albumin were given for four patients in the third and fourth months, they could not be confirmed on re-examination.

**Allergic Sensitivity:** Up to April 15, 1952, no signs of allergic sensitivity were noted in either group. About this time eight viomycin treated patients complained of angioneurotic edema, a generalized urticarial rash and

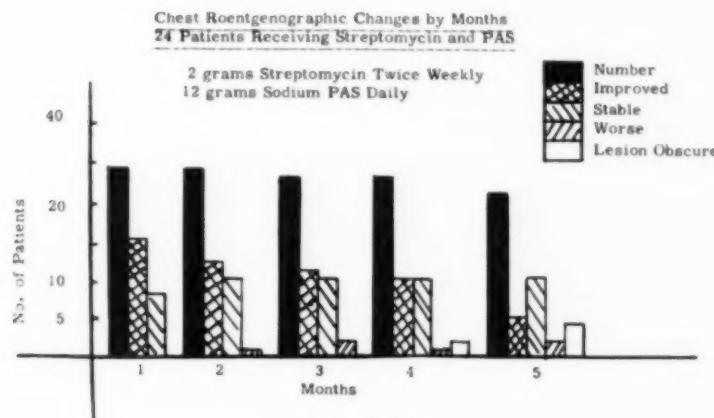


FIGURE 5

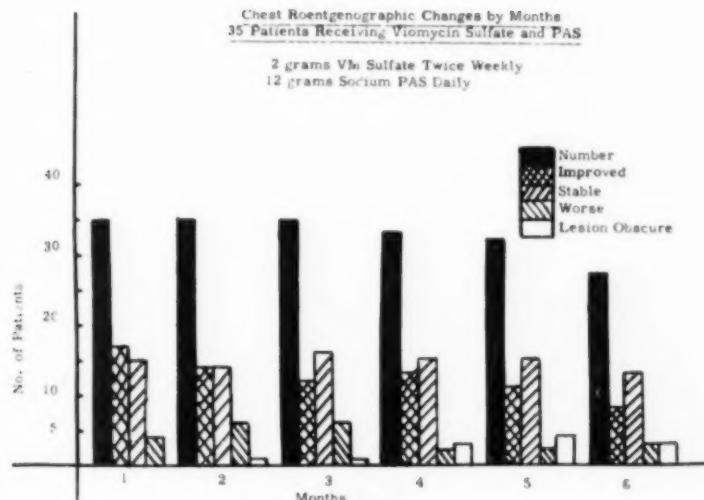


FIGURE 6

itching and burning at the site of injection. All of them experienced these symptoms within 24 hours after the injection.

All on viomycin were then changed to a new lot. No recurrence of these allergic symptoms were observed with the new lot of the drug.

Allergic sensitivity to streptomycin did not occur.

#### *Patients Resistant to Streptomycin*

For the seven patients initially resistant to streptomycin on starting viomycin treatment, the drug appeared clinically effective (Table IV). One improved sufficiently to have right pneumonectomy in the sixth month of treatment. Four still had organisms resistant to 100 mcg. of streptomycin after six months of viomycin treatment. The three other patients had negative cultures at this time.

#### *Bacterial Resistance to Viomycin*

Of 35 patients placed on viomycin, 25 had organisms sensitive to 5 mcg. of viomycin at the beginning of treatment. Nine had negative cultures of whom three had later cultures sensitive to 5 mcg. One was reported sensitive to 50 mcg. but not to 25 mcg. initially but in the third month of treatment was culture negative.

Out of 15 viomycin treated patients with five month culture reports, eight had negative cultures. Of the seven positive, six were sensitive to 5.0 mcg., and one is sensitive to 12.5 mcg. None of seven cultures positive patients became resistant to streptomycin.

#### *Sputum Conversion*

The sputum concentrates of streptomycin treated patients became negative more frequently in the early months of treatment and tended to remain so (Figure 3). Negative sputum concentrates were less frequent and less persistent among the viomycin treated patients (Figure 4).

Cultural results are not significant because of the large number not reported in the later months of observation.

#### *X-ray Improvement or Stability*

X-ray clearing of exudative lesions seemed more striking with streptomycin treatment (Figures 5 and 6). Viomycin treated patients showed definitive improvement but less frequently and less strikingly.

#### *Ambulatory Patients*

Four ambulatory patients receiving viomycin and PAS showed clinical improvement after six months of therapy. Three of them had moderate improvement of recent exudative spread and one showed healing of a tuberculous sinus of four years duration. Sputum was negative in all four at the beginning of treatment and remained so throughout the study.

#### *Clinical Improvement*

As already stated, seven patients having streptomycin resistant organisms showed clinical improvement with 2 grams of viomycin given twice weekly and 12 grams of PAS given daily (Table IV).

Staff opinions of the clinical effectiveness of viomycin rate it below streptomycin and better than PAS alone.

The influence of the drug on the systemic symptoms of tuberculosis is difficult to evaluate from this series. Fever was present initially in 11 of the viomycin treated patients. It became normal for all from two to six weeks after starting therapy. In 11 febrile streptomycin treated patients temperatures became normal in from one to four weeks. Body weight increased under treatment in both groups. There was little difference in the rate of weight gain between the two groups.

#### SUMMARY

- 1) Viomycin in doses of 2 grams twice weekly combined with 12 grams of PAS daily is of slight toxicity.
- 2) Tinnitus may be expected to occur. Allergic symptoms have not been a major problem. Auditory nerve damage of a serious degree is not frequent.
- 3) Streptomycin resistant organisms are affected by viomycin and patients having such organisms improve under intermittent viomycin treatment.
- 4) Bacterial resistance to viomycin did not develop to a significant degree among patients treated for six months.
- 5) Clinical and x-ray improvement is more striking in streptomycin-PAS treated patients, however, the effectiveness of viomycin-PAS is definite and demonstrable.
- 6) The clinical use of viomycin is feasible in the presence of streptomycin resistant organisms, and allergic sensitivity to streptomycin. Its use with newer antimicrobials should be explored.

#### RESUMEN

- 1) La viomicina a la dosis de dos gramos dos veces por semana combinada con 12 gramos de PAS diariamente, es de ligera toxicidad.
- 2) Tinitus puede ocurrir. Los síntomas alérgicos, no han sido un problema de consideración. El daño al nervio auditivo en grado serio no es frecuente.
- 3) Los organismos estreptomicino-resistentes, son afectados por la viomicina y los enfermos que tienen tales organismos, mejoran bajo la tratamiento intermitente de viomicina.
- 4) Entre los enfermos tratados durante seis meses, no se desarrolló al viomicino-resistencia en grado significante.
- 5) La mejoría clínica y radiológica, es más notable en los enfermos tratados con estreptomicina-PAS; sin embargo, la efectividad de la viomicina es definida y demostrable.
- 6) El uso clínico de la viomicina, es practicable en presencia de organismos estreptomicino-resistentes y ante la sensibilidad alérgica la estreptomicina. Su uso con los más recientes antibióticos, debe investigarse.

#### RESUME

- 1) La viomycine à la dose de deux grammes, deux fois par semaine, associée à 12 grammes de P.A.S. par jour est de faible toxicité.

- 2) Des tintements d'oreille peuvent apparaître. Il n'y a pas de problème majeur posé par des signes d'intolérance. Les atteintes graves du nerf auditif ne sont pas fréquentes.
- 3) La viomycine agit sur les microbes résistants à la streptomycine. Les malades porteurs de tels bacilles sont améliorés lorsqu'il sont soumis au traitement par la viomycine.
- 4) Il n'apparaît pas un degré important de résistance bactérienne à la viomycine chez les malades traités pendant six mois.
- 5) L'amélioration clinique et radiologique est plus frappante pour les malades traités par la streptomycine et le P.A.S. bien que l'action de la viomycine associée au P.A.S. est certaine et peut être démontrée.
- 6) L'utilisation clinique de la viomycine est efficace dans les cas où les bacilles sont streptomycino-résistants, ou lorsque les malades sont intolérants à la streptomycine. Son action devrait être étudiée en conjonction avec les nouveaux produits antimicrobiens.

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## Dramamine (Dimenhydrinate) as an Adjunct to PAS (Para-aminosalicylic Acid) in the Treatment of Pulmonary Tuberculosis

LESTER I. LEONARD, M.D.\*

Lantana, Florida

The treatment of pulmonary tuberculosis has changed so radically in the past few years that we are now able to alleviate symptoms, save lives that were previously doomed, bring acute and far-advanced cases to surgery as a definitive form of therapy and even help to prevent operative and post-operative complications in a manner never before experienced. This has come to pass through the administration of medications which have just recently climbed the therapeutic horizon. One of the newer regimens of proved therapy has been the so-called "combined therapy" consisting of streptomycin, PAS (para-aminosalicylic acid) and pneumoperitoneum or some other form of pulmonary relaxation in addition to bed rest. Of these three components streptomycin has perhaps produced the most dramatic results and yet none of these alone has been able to equal the therapeutic effect obtained by the combination of all three together.<sup>1</sup>

Through the maze of trial and error in experience, certain changes in the usage and dosage<sup>2</sup> of these drugs (streptomycin and PAS) have brought about a reduction and even complete absence of specific undesirable reactions.<sup>3-7</sup> The dose of streptomycin has been decreased in amount as well as in frequency of administration<sup>8</sup> in order to prevent eighth nerve toxicity as well as to delay resistance of organisms to the drug. Another form of streptomycin, namely dihydrostreptomycin,<sup>9</sup> has also been utilized for the same purpose with equivocal success.

PAS which has been proved to be of value by itself,<sup>10-13</sup> *in vivo* as well as *in vitro* in combatting tuberculosis, also may produce toxic reactions which are undesirable. Many of us who have worked with it for any length of time have witnessed the patient who suddenly complains of symptoms which seem to fall into three definite groups. One group appears to exhibit an irritation of the upper gastrointestinal tract (U.GI) with such symptoms as fullness, eructations, anorexia, nausea and vomiting. The second group apparently reveals an irritation of the lower gastrointestinal tract (L.GI) with frequency of watery stools (up to 12 to 15 per day). The third group shows overlapping or combination of symptoms of the two former groups. It would appear that some inherent factor in the host is responsible for this difference. All three groups may show progressive weight loss despite x-ray film and clinical improvement. These symptoms may often be troublesome enough to make PAS intolerable.

Despite these toxic manifestations the increasing evidence of its impor-

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tance in the scheme of treatment both for its own effect upon the tubercle bacillus as well as for its aid in preventing the emergence of resistance of some of the tubercle bacilli to streptomycin<sup>14,15</sup> (especially in cavitary and far-advanced disease with a large total area of involvement) led us to again modify the usage, dosage and administration of PAS rather than to give up its use. Various drugs were used in an attempt to relieve these symptoms without success. Assuming that the acid radical was the cause of the gastrointestinal irritation various methods of neutralization have been devised. Sodium bicarbonate tablets (gr. x) were given together with each dose of PAS powder. Other patients received an aqueous solution of PAS, sodium bicarbonate together with some flavoring agent. Finally sodium PAS was introduced as a neutralized ion. (The PAS powder used here at the Southeast Florida Tuberculosis Hospital is supplied by Merck and Company, Rahway, N. J., the Sodium PAS by the Consolidated Midland Company, Katonah, N. Y.). There seemed little doubt that the addition of alkali generally increased the patient's tolerance to PAS and therewith a greater number of patients were able to tolerate larger doses (12 to 20 Gms./day). However the use of the soda tablets by themselves required the ingestion of a large amount of medication per day. The procedure of making the solution leaves much to be sought for with the necessity for a container which is much larger than the total fluid volume because of the gaseous escape as well as the length of time it takes for the completion of this reaction. The sodium PAS theoretically sounded logical yet proved to be no better than acid PAS in our hands. Another obstacle which arose was the growing mass of evidence that neutralized PAS is less effective upon the tubercle bacillus than is the ordinary acidic PAS.

Enteric coated PAS has also been used. Although this method of administration also required the ingestion of a great number of pills daily, it is of some value to patients unable to tolerate the powder. More recently PAS

TABLE I: TOLERANCE TO ACID PAS POWDER WITH NaHCO<sub>3</sub>

	Tolerated PAS Well	Tolerated PAS Well Only With Dramamine	Not Helped by Total Dramamine	
Total on Drug	108	91	14	3
Per cent of Total	100	84.2	12.9	17
			2.8	15.7

TABLE II: SYMPTOMS WITH ACID PAS POWDER AND NaHCO<sub>3</sub>

	*UGI	*LGI	U and LGI	Total Having Intolerable Symptoms
Total on Drug	108	5	8	17
Per cent of Total	100	4.6	7.4	15.7
Per cent of Sym- tomatic Group	29.4	47.0	23.6	100

\*UGI = Symptoms referable to Upper GI Tract.

\*LGI = Symptoms referable to Lower GI Tract.

has been administered per rectum<sup>16</sup> with unconfirmed success so far as tolerance and effect are concerned. Thus we were still confronted with the fact that all our patients were receiving PAS which was not as effective as the ordinary PAS as well as a group of patients (15.7 per cent) who either could not take the drug at all, were taking it but not eating well and losing weight or were taking it and were not necessarily losing weight but were just plain miserable because of the toxic symptoms.

Rather recently we decided to assay the value of dramamine (brand of dimenhydrinate, G. D. Searle and Co., Chicago, Ill.). Previously it was used chiefly in types of gastrointestinal syndromes that were of a reflex nature such as air and sea-sickness. Scattered initial reports of success in post-operative nausea and vomiting have not as yet been confirmed. At any rate it was first decided to merely assay its efficacy, if any, in a few desperate cases of pulmonary tuberculosis who previously had been unable to take PAS at all despite the fact that they needed it most, either in conjunction with some other therapy or alone because all other forms of treatment had been exhausted in the face of progressive disease.

Following uniform success with three patients who had previously been unable to tolerate PAS because of intractable gastrointestinal disturbance, it was decided to obtain sufficient dramamine to use routinely in all patients who encountered difficulty in tolerating PAS. The powdered acidic PAS was used in all cases except for a period of one month when sodium PAS was prescribed. Patients received the acid PAS powder in three divided doses after meals varying from a daily total of 12 to 18 Gms. in whatever liquid they desired. Invariably after experimenting with different liquids most of the patients used plain tap water. Sodium bicarbonate in doses of 10 grains was given with each dose of PAS. As soon as a patient complained of symptoms the PAS was routinely discontinued for 24 hours and then reinstated. If no further complaints were made the PAS was continued

TABLE III: TOLERANCE TO SODIUM PAS

		Tolerated PAS Well	Tolerated Sodium PAS Poorly	Helped by Dramamine
Total on Drug	38	16	22	3
Per cent of Total	100	42	58	7.8

TABLE IV: SYMPTOMS WITH SODIUM PAS

		*UGI	*LGI	U and LOI	Total Having Intolerable Symptoms
Total on Drug	38	0	10	12	22
Percent of Total	100	0	26.3	31.5	58
Per cent of Sympto- matic Group		0	45.4	54.5	100

\*UGI = Symptoms referable to Upper GI Tract.

\*LGI = Symptoms referable to Lower GI Tract.

as planned. If the same patient complained a second time the PAS was discontinued and omitted for 48 hours and then reinitiated routinely. If the same individual complained a third time the PAS was again omitted for 48 hours and then restarted with dramamine. This was given in 50 mgm. doses t.i.d. one hour before meals. In carrying out this scheme in the first 10 patients requiring dramamine, it was discontinued three days after uneventful administration of PAS. Invariably the patient soon renewed his former complaints and the dramamine was administered thereafter throughout the course of the PAS. Because of this uniformity none of the other 98 cases on PAS with sodium bicarbonate were put through this last phase of temporary omission of the dramamine.

No patient was given dramamine unless there occurred a repetition of symptoms severe enough to cause misery or continued weight loss. Such symptoms as persistent frequency of watery stools, loss of weight or inability of a cachectic patient to gain weight because of anorexia, protracted nausea and vomiting not associated with cough or of a reflex nature were all felt to be ample indication for its use. Fullness, tolerable nausea, occasional vomiting and diarrhea and controllable "heartburn" were not considered important enough to warrant the use of dramamine.

One hundred and eight male patients were followed through their course of acidic PAS powder with sodium bicarbonate pills. All of them were also taking streptomycin (Gms. 1 every three days) and all but five were taking pneumoperitoneum. Of these five, one was taking left pneumothorax and the other four were not receiving any active form of pulmonary relaxation other than bed-rest. These factors apparently had no effect upon the tolerance to PAS. One hundred and eight patients were followed through a three to six months course of ordinary acidic PAS. Thirty-eight were also followed through a one month course of sodium PAS.

Of the 108 patients on acid PAS powder with sodium bicarbonate pills 91 (84.2 per cent) tolerated the drug well but a significant number, 17 (15.7 per cent) experienced repeated symptoms so severe that the administration of PAS became intolerable. With dramamine 14 of these 17 patients could tolerate the PAS well and finished their course uneventfully. Their symptoms did not always disappear completely but enough so that the PAS was well tolerated. The other three were also put on dramamine but because of intolerable symptoms both PAS and dramamine had to be discontinued. Two of these were not helped at all by the dramamine and the other refused to take the drug because it made him drowsy and he felt that he was being "doped". Most of the other patients receiving dramamine seemed to welcome this side effect of drowsiness. Thus of the 17 needing dramamine, three (17 per cent) were not helped; 14 (83 per cent) were definitely aided enough so that they could continue and complete their course of PAS.

In the group of 17 patients experiencing severe gastric intestinal symptoms, the complaints of symptoms referable to the lower gastro intestinal tract were more common. Of these 17, four (23.6 per cent) had symptoms of both upper and lower gastrointestinal irritation.

Of the 38 patients taking sodium PAS alone only 16 (42 per cent) tolerated it well. (Two of these 16 actually preferred it to the acidic PAS with sodium bicarbonate). Twenty-two (58 per cent) found the sodium PAS intolerable. Only three (13.6 per cent) of this symptomatic group of 22 were helped by dramamine enough to make the sodium PAS tolerable.

In the group of 22 patients on sodium PAS who experienced intolerable symptoms none complained of symptoms referable to the upper gastrointestinal tract alone. Twelve (54 per cent) complained of symptoms referable to both the upper and lower tract simultaneously while 10 (45 per cent) complained of symptoms referable to the lower gastrointestinal tract alone.

#### *Discussion*

Certain definite conclusions have resulted from these observations which seem worthwhile in order to evaluate the effect of the administration of PAS in the treatment of pulmonary tuberculosis. For instance eight of 108 patients on PAS (7.4 per cent) admitted that they frequently did not take their PAS for a week at a time because of gastrointestinal symptoms. This occurred despite the fact that the medication was reported as having been administered. If this 7.4 per cent was added to the 15.7 per cent who reported intolerance to PAS, we would have a total of 23 per cent of patients receiving the drug who found it intolerable. Thus it would seem that closer observation, questioning and explanation of the importance of taking the PAS is necessary in order to obtain an accurate picture of tolerance to PAS. This fact might explain, perhaps, why the experience of some readers might differ with my own.

Although it is generally felt that 10 to 20 Gms. of PAS per day is required for a therapeutic dose it would be interesting to know the minimal amount that is required daily to help prevent the emergence of resistance of the tubercle bacillus to streptomycin. If this fact was available it might be better to administer just enough PAS with the streptomycin to prevent resistance, in the group of patients unable to tolerate the present therapeutic dose. This would obviate the gastrointestinal symptoms at the expense of some of its therapeutic effect. I am not aware that this dosage has been established, as yet, for clinical use.

Only one of the 108 patients on PAS had an antecedent history of gastrointestinal disease. He had had a gastro-enterostomy nine years previously. After showing a complete intolerance to acid PAS with dramamine in the fact of culture resistance of his organisms to streptomycin, he was given enteric coated PAS uneventfully but succumbed to his disease six weeks after the course was started. The onset of toxic symptoms to PAS followed no time pattern. However only two of the patients experienced ill effects before the 10th day of therapy. From then on the onset was unpredictable.

Using the present dosage a significant number, 17 (16 per cent) of patients taking acid PAS with sodium bicarbonate (108 total) suffered intolerably and 14 (82 per cent) of these were definitely helped by the use of dramamine. The large number of patients (58 per cent) who found the

sodium PAS intolerable was surprising. The fact that only three (13.5 per cent) of these were helped by dramamine was also unexpected.

However as long as PAS remains as an adjunct in the treatment of pulmonary tuberculosis, whether by itself or in conjunction with other medication or relaxation therapy, it would seem that dramamine is of definite value in those patients who suffer toxic symptoms and find the PAS to be intolerable. Sodium PAS is not tolerated well and dramamine is of little help in increasing the patients' tolerance to it.

#### SUMMARY

- 1) Acid PAS with sodium bicarbonate is tolerated much better than is sodium PAS and when toxic symptoms appear they are much more severe with the sodium PAS.
- 2) A significant group of patients taking PAS in the treatment of pulmonary tuberculosis find it intolerable (16 per cent of this group).
- 3) Statistics on tolerance are difficult to evaluate since patients are known to discontinue the medication by themselves because of gastrointestinal symptoms without reporting it.
- 4) Dramamine is of value in relieving the intolerable toxic symptoms experienced by some of the patients taking PAS with  $\text{NaHCO}_3$  and is therefore recommended for this purpose (14 of 17 or 83 per cent were helped in this study).
- 5) Dramamine is of little help in relieving the symptoms caused by sodium PAS in some patients (only three or 13.5 per cent of those experiencing symptoms were aided in this study).
- 6) Drowsiness is a common side reaction and is the only one experienced in the clinical use of dramamine.

#### RESUMEN

- 1) El PAS ácido con bicarbonato de sodio, es mucho mejor tolerado que el PAS sódico y cuando aparecen síntomas tóxicos con este último, parece que son mucho más severos.
- 2) Un número significativo de enfermos que toman PAS en el tratamiento de la tuberculosis pulmonar, lo encuentran intolerable (16 por ciento de este grupo).
- 3) Las estadísticas sobre la tolerancia, son difíciles de estimar pues, se sabe que hay enfermos que interrumpen la medicación por si mismos a causa de trastornos intestinales y no lo refieren.
- 4) La dramamina, es de valor para aliviar los síntomas tóxicos intolerables, que algunos enfermos experimentan cuando toman PAS con bicarbonato de sodio y por tanto, se recomienda para ese fin (14 o 17 u 83 por ciento, fueron aliviados en este estudio).
- 5) La dramamina, es de poco valor para aliviar los síntomas causados por el PAS sódico en algunos enfermos (sólo 3 o sea el 13.5 por ciento de los que tuvieron síntomas, mejoraron según este estudio).
- 6) La somnolencia, es una reacción común y es la única experimentada con el uso clínico de la dramamina.

## RESUME

1) L'acide P.A.S. absorbé avec du bicarbonate de soude est bien mieux toléré que le P.A.S. sodique et lorsqu'il y a des accidents toxiques, ils sont plus importants quand on utilise le P.A.S. sodique.

2) Un groupe important de malades à qui l'on administrait du P.A.S. pendant le traitement de la tuberculose pulmonaire ne purent le supporter (16%).

3) Il est difficile d'établir des statistiques sur la tolérance depuis qu'on sait que les malades interrompent sans le dire la médication de leur propre chef, à cause de troubles gastrointestinaux.

4) La dramamine est un médicament de valeur pour combattre les symptômes toxiques d'intolérance. Après avoir été expérimentée sur quelques-uns des malades absorbant du P.A.S. avec du bicarbonate de soude, elle est conseillée dans ces cas.

5) La dramamine n'est que d'un petit secours pour combattre les symptômes dûs au P.A.S. sodique, chez les quelques malades où on a du l'utiliser.

6) La somnolence est une complication habituelle et la seule qu'on ait notée.

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## Stress in Pulmonary Tuberculosis\*

I. Thorn Test and Circulating Eosinophils in Surgical Patients.

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Stress in pulmonary tuberculosis is not now well defined. In the past, the alterations in the formed elements of the blood, changes in the sedimentation rate and a variety of immunological reactions have been investigated especially to determine the pre-surgical status or activity of the tuberculous infection. In 1943, Muller,<sup>1</sup> at the Massachusetts Rutland State Sanatorium, made an exhaustive study of these factors. This book indicates that a need existed for clinical tests to estimate the ability of the tuberculous patient to withstand surgical therapeutic measures. These authors emphasized especially the use of changes in the formed elements of the blood as a possible prognostic tool to judge the state of balance of the tuberculous infection and they utilized blood examinations to estimate the patient's ability to localize his disease. Such studies give hematological measurements of the host's response to invasion by tubercle bacilli. Pinner,<sup>2</sup> in 1945, discusses further immunological, pathological and allergic aspects of the host's response.

Recently with the understanding of the General Adaptation Syndrome,<sup>3,4</sup> the importance of adrenal function has been emphasized in the mechanisms of resistance in infection,<sup>5</sup> cold,<sup>6,7</sup> heat,<sup>8,9</sup> work,<sup>10</sup> and surgical trauma.<sup>11-13</sup> Adrenal function as an important factor in infection and immunity would appear to require more testing and correlation with the clinical behavior of diseases such as tuberculosis.

We undertook a study which measured adrenal function in patients with chronic pulmonary tuberculosis. The Thorn test was evaluated as an aid to predict preoperatively the response of tuberculous patients to the stress of surgical treatment. Because of the importance of surgery in the clinical management of pulmonary tuberculosis and because surgery produces an acute stress, a large number of patients undergoing major surgery were studied.

**Material and Methods:** One hundred ten patients having chronic pulmonary tuberculosis were studied, 81 of whom were subjected to surgery during the investigation, and 29 received medical therapy alone. Although at three month intervals for two years, the following determinations and evaluations were made, only the pertinent data relating to adrenal function

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as measured by circulating eosinophils and the Thorn test are being reported here.

1. Thorn test.
2. Postoperative circulating eosinophils.
3. Serum proteins.
4. Circulating blood volume.
5. Sedimentation rate.
6. Cephalin flocculation and thymol turbidity liver function tests.
7. Complete blood counts and hemoglobin determinations.
8. Numerical estimation of the extent of the tuberculous infection in each individual case.
9. Data was subjected to analysis by well recognized statistical methods.<sup>14</sup>

#### *The Prognostic Significance of the Thorn Test*

*Theory:* The prognosis in chronic pulmonary tuberculosis can be considered as a struggle between the invasive forces of the tubercle bacillus and the resisting forces of the host. A relatively small stress may upset the balance between host and parasite and so turn the tide of battle to favor either the infecting organism or the resisting host. In this prolonged struggle the treatments themselves may constitute a stress which becomes part of the combat being waged by the host against the parasite. The surgical treatment of pulmonary tuberculosis produces stress responses which can be readily studied.<sup>15</sup>

When the adrenal glands are depleted of hormone, partially destroyed or hypofunctioning, the individual subjected to stress may be deprived of a host of protecting hormonal substances, which influence protein,<sup>16</sup> carbohydrate, mineral, water and cell membrane metabolism. The discussion of all these factors in the General Adaptation Syndrome is beyond the scope of this paper, despite their obvious importance. Selye's books<sup>3,4</sup> review the subject in detail. Finley, et al<sup>17</sup> imply that lowered adrenal reserves in patients with pulmonary tuberculosis undergoing surgical treatment might be associated with increased frequency of postoperative complications. With this concept in mind, we correlated the preoperative Thorn test<sup>18,19</sup> with the occurrence of postoperative complications. In addition we compared the stress response produced by different surgical procedures.

*Material and Method:* The Thorn test is a determination of the percentage drop in circulating eosinophils following administration of ACTH. An eosinophil count of blood drawn from the finger tip is made in the afternoon. Then 25 mgs. of ACTH\* is given intramuscularly, and in four

\*The ACTH used in this study was supplied by Armour & Co. In the course of administering 446 individual doses of ACTH, it is not surprising that an occasional drug reaction to ACTH should appear. Twenty-two instances of allergy to pork ACTH have been reported,<sup>23-28</sup> one of them being a contact dermatitis,<sup>29</sup> and one an allergy to beef ACTH.<sup>29</sup> All the ACTH used in our study was derived from the hog. We had three instances of allergic reactions to a single 25 mgm. dose of ACTH, one occurring after the first injection of the drug and the other two following the third dose. In one instance the reaction was severe enough to require the use of adrenalin and intravenous benadryl. In the other two instances in which urticaria and maculo-papular rash appeared, oral dosage of an anti-histamine adequately controlled the symptoms.

hours the eosinophil count is repeated. The direct chamber method of Randolph<sup>20</sup> was used. The percentage fall of the circulating eosinophils, after administration of ACTH, is a reliable measure of adrenal responsiveness.<sup>18-22</sup> A preoperative fall of less than 35 per cent in circulating eosinophils following injection of 25 mgs. of ACTH constitutes evidence of lowered adrenal reserves.<sup>18</sup> In a few selected instances 50 mgs. of ACTH were used as the testing dose.

Eighty-one consecutive cases coming to surgery were divided into three groups:

1. Pneumonectomy.
2. Limited pulmonary resection.
3. Surgical collapse procedures.

Each main group was subdivided into postoperative complicated and uncomplicated cases.

If lowered adrenal function were a factor in the occurrence of complications, then the uncomplicated cases should have preoperative Thorn tests which fell in the normal range (35 to 100 per cent), while many of the cases with postoperative complications would be expected to have low (below 35 per cent) preoperative Thorn tests. To find the lower limit of the range of Thorn test results in the uncomplicated cases, these values were placed into a "100 per cent Normal Probability Curve."<sup>\*\*14</sup>

The correlation between poor adrenal function and postoperative complications was determined in the following way. Considerations which were not related to adrenal responsiveness were removed, such as gross hemorrhage from a thoracic vessel, respiratory insufficiency associated with pneumonectomy, and overwhelming tuberculous infections. The predicted number of complications in each surgical group was compared with the actual number of complications which occurred.<sup>†</sup>

**Findings:** A control group of 28 normal individuals was studied, all of

<sup>\*\*</sup>We arbitrarily decided that any response on the curve which fell below the 10 per cent mark, starting from the negative side of the curve, would be considered as a poor result of Thorn test. Statistically, this is a severe test of biological data. <sup>†</sup>The Chi Square test of the Reliability of Percentages<sup>14</sup> was used to calculate this number of predicted complications. The formula of the Chi Square test determines the expected number of complications from the ratio of the number of uncomplicated cases to the total number of cases in the series.

CHART I: THORN TEST IN NORMAL INDIVIDUALS AND IN PATIENTS WITH CHRONIC PULMONARY TUBERCULOSIS

	GOOD THORN TEST		POOR THORN TEST	
	Above 35 Per cent Number	Per cent	Below 35 Per cent Number	Per cent
Control Group (Normal)	28	100	0	0
Entire Group of 110 Tuberculous Patients	85	77.3	25	22.7
81 Cases Having Surgery	62	77	19	23

whom had good Thorn tests (over 35 per cent). In the entire group of 110 tuberculous patients, 25 (22.7 per cent) had poor Thorn tests (below 35 per cent), and in the 81 cases having surgery there were 19 (23 per cent) with poor Thorn tests (Chart I).

The statistical pattern of the Thorn test range of this entire group is within the normal range established by Thorn.<sup>18</sup> Fifty-nine of the consecutive 81 operative cases made up the uncomplicated surgical group. All but seven had good Thorn tests. It appeared that the uncomplicated cases had good adrenal function (Chart II).

There were five deaths and 17 instances of morbidity which make up the group of patients with postoperative complications. Sixteen per cent of the cases with *good* Thorn tests had complications, while 63 per cent of the patients with *poor* Thorn tests, had complications (Chart III).

<sup>†</sup>Blood volume—The tendency to surgical shock is greater in the individual with a contracted blood volume.<sup>38</sup> In people *undergoing bed rest alone*<sup>39</sup> as well as in patients with tuberculosis<sup>40</sup> treated with bed rest, diminished circulating blood volumes were found. If preoperative circulating blood volume deficits, as determined by Evans Blue,<sup>41-44</sup> are raised to normal and blood loss during surgery estimated by a gravimetric method<sup>45-47</sup> is replaced, the effect of blood loss in the production of surgical shock might be minimized. Fifty-two (47.3 per cent) of the 110 patients with tuberculosis were found to have initial or preoperative contracted blood volumes—the deficits ranged from 750 to 3000 ccs. We could find no correlation between circulating blood volume deficits and adrenal function (Thorn test), clinical activity of the patient's tuberculosis, the prognosis of the individual case, or the ability of the individual to withstand surgery once the circulating deficit was corrected.

CHART II: PREOPERATIVE THORN TEST  
59 UNCOMPLICATED SURGICAL CASES

Type of Surgery	Uncomplicated Cases	Mean	Standard Deviation	(Upper 90 Per cent of Scale)* Normal Range
Pneumonectomy	10	69.0	24.2	37.8 - 100
Limited Resections	32	62.2	24.6	**31.5 - 100
Thoracoplasty	17	63.3	19.7	37.9 - 100
<b>TOTAL</b>	<b>59</b>			

\*See footnote \*\*, Page 62.

\*\*Seven of these 32 limited resection cases had Thorn test values below 35 per cent.

CHART III: COMPARISON OF THORN TEST VALUES IN UNCOMPLICATED AND COMPLICATED SURGICAL CASES

THORN TESTS Over 35 Per cent No. Pct.			THORN TESTS Below 35 Per cent No. Pct.		
<i>Uncomplicated Cases:</i>					
59 cases	52	84	7	37	
<i>Complicated Cases:</i>					
Mortality	5 cases	10	3	4.8	
Morbidity	17 cases	7	11.2	16	
			12	2	10.5
				10	52.5
<b>TOTAL</b>		<b>62</b>	<b>67</b>	<b>19</b>	<b>23</b>

If complications with some obvious explanation (large pulmonary artery hemorrhage,<sup>11</sup> etc.) are removed from the compilation of *expected* complications in individuals with low Thorn tests, then the calculated incidence of *expected* complications is 62.7 per cent. The *actual* number of cases with poor Thorn tests which developed postoperative complications, not from an obvious cause, and which we considered *might* be due to stress was 12 (63 per cent).

Patients with postoperative gastric hemorrhage, thrombophlebitis, ileus, acidosis, allergic reactions and nerve muscle paralysis, represent examples of complications occurring without obvious causes. Such postoperative occurrences have been suspected to be associated with the Alarm Reaction.<sup>3,4</sup> We cannot be certain from our own data if such complications are manifestations of the Alarm Reaction, but there is indirect evidence that they may be. Thus, all of the complications with no obvious explanation, appeared in the group with poor Thorn tests, whereas in the group with good Thorn tests, the complications had some obvious explanation, such as gross hemorrhage, respiratory insufficiency or infection (Charts IV and V). The only deviation between expected and actual occurrence of complications was found in the pneumonectomy group where nine complications occurred and eight were expected. In the limited resection and surgical collapse groups, the number of actual and expected complications (Chart VI) was the same.

*Significance:* A Thorn test of below 35 per cent is a reliable indication of lowered adrenal responsiveness. There is a 23 per cent incidence of lowered adrenal responsiveness in a representative group of patients with chronic pulmonary tuberculosis. Sixty-three per cent of the patients with poor Thorn tests coming to surgery developed some type of postoperative complication. From our data it would appear that stress complications occur almost always in individuals with poor Thorn tests as shown by the fact that the range of Thorn tests in the uncomplicated groups was 35 per cent or over. As with all biological testing, variable results may be obtained with different group sampling, but certainly the Thorn test would seem to be a most valuable adjunct in preoperative evaluation of doubtful surgical cases.

CHART IV: MORTALITY (FIVE CASES) OCCURRING IN 81 CONSECUTIVE SURGICAL CASES CORRELATED WITH THE THORN TEST

Complication	THORN TEST Above 35 Per cent	THORN TEST Below 35 Per cent
Non-hemorrhagic Shock		2 cases
Severe Hemorrhage (Hepato-Renal Syndrome)	1 case	
Pulmonary Insufficiency (Cystic Disease)	1 case	
Pulmonary Vein Thrombus with Embolus	1 case	

*Stress Reaction to Surgery as Measured by the Postoperative Circulating Eosinophilic Response*

*Theory:* Sufficient evidence exists to state that the percentage fall of circulating eosinophils postoperatively indicates the severity of the "stress reaction," and that the duration in days of eosinophilic fall indicates the duration of the stress.<sup>31-34</sup> This eosinophilic response could be used to evaluate the severity of the "stress" produced by various surgical procedures. If thoracoplasty produced less stress than lobectomy, such information might be useful in choosing an operative procedure for the doubtful risk cases. Furthermore, if the force of one surgical procedure produced a more sustained outpouring of adrenal hormones than another, the possibility exists that spread of tuberculosis might be facilitated, just as a spread of tuberculosis has been reported associated with ACTH or cortisone therapy.<sup>35-37</sup>

CHART V: MORBIDITY (17 CASES) OCCURRING IN 81 CONSECUTIVE SURGICAL CASES CORRELATED WITH THE THORN TEST

Complications	THORN TEST Above 35 Per cent	THORN TEST Below 35 Per cent
Bronchopleural Fistula	4 cases	
Postoperative Spread	2 cases	1 case
Shock, Non-hemorrhagic		3 cases
Severe Hemorrhage	1 case	
Penicillin Allergy		1 case
Postoperative Ileus		1 case
Thromboplebitis		1 case
Gastric Hemorrhage		1 case
Diabetic Acidosis		1 case
Muscular Palsy		1 case
<b>TOTAL</b>	<b>7 cases</b>	<b>10 cases</b>

CHART VI  
THE THORN TEST AS A PROGNOSTIC TOOL IN PREDICTING POST-OPERATIVE COMPLICATIONS IN 81 CONSECUTIVE SURGICAL CASES

	19 cases	Uncomplicated Cases		Complicated Cases	
		*Expected	Actual	*Expected	Actual
Pneumonectomy	19 cases	11	10	8	9
Lobectomy					
Segmental					
Thoracotomy	42 cases	32	32	10	10
Thoracoplasty	20 cases	17	17	3	3
<b>TOTAL</b>	<b>81 cases</b>	<b>60</b>	<b>59</b>	<b>21</b>	<b>22</b>

\* Calculated Statistically.

**Method:** A preoperative circulating eosinophil count was done on blood drawn from the finger tip and repeated on each postoperative afternoon until the count had returned to preoperative levels for two days.

The uncomplicated surgical cases were grouped into categories as to operative procedure. The average and standard deviation in the percentage fall and days' duration fall of circulating eosinophils was calculated. The complicated cases were grouped together rather than being separated according to types of surgery for the convenience of having a statistically significant group to compare to the uncomplicated groups. The eosinophilic response between the first and second stage of thoracoplasty in eight cases was compared. The data so obtained was analyzed by testing for the Significance of Difference Between Means.<sup>14</sup>

**Findings:** In the uncomplicated cases no significant difference in stress, as measured by the extent and duration of fall of circulating eosinophils, was found after pneumonectomy, limited resection and first stage thoracoplasty. Although the means of the fall and duration of fall of eosinophils were greater in pneumonectomy cases than limited resection cases and least in the first stage thoracoplasty, the standard deviation brought these values all into the same range (Chart VII).

In complicated cases the mean percentage fall of circulating eosinophils was essentially the same as in the uncomplicated cases. However, the duration of the eosinophilic fall averaged 5.2 days in the group with complications while the duration fall in the uncomplicated groups was less, 3.4 days for thoracoplasty to 4.2 days for pneumonectomy (Chart VII).

We observed two instances of postoperative shock following mild surgical trauma in which the Thorn test had indicated no adrenal reserve (0 per cent Thorn test) and the postoperative circulating eosinophils showed no fall at all.

The first patient, A.G., a 43 year old white male, underwent a revision of an Eloesser Flap, draining an empyema space. His blood pressure began

CHART VII  
POSTOPERATIVE EOSINOPHILIC RESPONSE OF 81 SURGICAL CASES

Type of Surgery	No. Cases	Per cent Fall in Circulating Eosinophils		No. Days Duration Eosinophils Below Pre-operative Levels	
		Mean	Stand. Dev.	Mean	Stand. Dev.
Pneumonectomy	10 cases	92	11.3	4.2	1.17
Limited Resection	32 cases	81	24.2	3.8	1.13
1st Stage Thoracoplasty	17 cases	77	21.1	3.4	1.15
2nd Stage Thoracoplasty	8 cases	80	22.2	5.1	1.14
Postoperative* Complications	22 cases	88	23.1	5.2	1.16

\* See Charts IV and V.

to fall at the end of surgery and was restored only after prolonged intravenous administration of Nor-Adrenalin. The second patient, E.G., a 38 year old white female, went into profound shock several hours after a second stage cavity drainage operation. The blood pressure was restored with intravenous Nor-Adrenalin. The total amount of blood loss in both these patients was not considered to be enough to cause the shock which resulted.

The eosinophilic response after the second stage of thoracoplasty was of the same intensity, but 1.7 days longer in duration than after the first stage of thoracoplasty, indicating that as in the complicated group of cases, stress response continued for a longer period of time (Chart VII).

*Significance:* It would appear that in individuals with good adrenal responsiveness the resistance of the host to the force of pneumonectomy, lobectomy and thoracoplasty, stress is essentially the same. This would imply that there exists a basic stress response which is elicited by all the operations under scrutiny. Despite the fact that one would expect the stress response to be greater after pneumonectomy than thoracoplasty, it apparently is not, at least as far as measurements by circulating eosinophils are concerned in uncomplicated patients.

Where complications occur and where adrenal reserves have been altered by a recent trauma (second stage thoracoplasty) the adrenal responses are longer in duration.

#### SUMMARY

- 1) Twenty-five (22.7 per cent) of 110 patients with chronic pulmonary tuberculosis were found to have low Thorn tests.
- 2) Nineteen (23 per cent) of 81 patients undergoing surgery for tuberculosis had low Thorn tests.
- 3) Twelve (63 per cent) of 19 patients with low Thorn tests undergoing surgery had postoperative complications probably related to poor adrenal response.
- 4) The preoperative Thorn test appears to be one of the aids when taken in conjunction with other clinical and laboratory findings, for assaying the ability of patients with chronic pulmonary tuberculosis to withstand surgery.
- 5) Studies of circulating eosinophils after pneumonectomy, limited resection and thoracoplasty indicate that an adrenal stress response of similar magnitude is set up by all three operations.
- 6) Second stage thoracoplasty produced a significantly more prolonged adrenal stress response than pneumonectomy, limited lung resection, or first stage thoracoplasty.

#### RESUMEN

- 1) Entre 110 enfermos con tuberculosis pulmonar crónica, 25 o sea el 22.7 por ciento se encontró que tenían pruebas de Thorn bajas.
- 2) Entre 81 enfermos que se sujetaron a la cirugía por tuberculosis, 19 (23 por ciento) tenían pruebas de Thorn bajas.

3) El 63 por ciento (12 enfermos) de 19 que se sujetaron a la cirugía tuvieron complicaciones postoperatorias, probablemente en relación con deficiente respuesta suprarrenal.

4) La prueba preparatoria de Thorn, parece ser una ayuda cuando se asocia a otros datos clínicos y de laboratorio, para explorar la capacidad de los enfermos con tuberculosis crónica para soportar la cirugía.

5) Los estudios de los eosinófilos circulantes después de la neumonectomía, o de resecciones limitadas o después de toracoplastia, indican que una respuesta suprarrenal de esfuerzo es de similar magnitud en las tres operaciones.

6) La toracoplastia de segundo tiempo produjo una respuesta prolongada mayor suprarrenal de esfuerzo que la neumonectomía, y que la resección parcial o que la toracoplastia de primer tiempo.

#### RESUME

1) Les auteurs ont découvert que parmi 110 malades atteints de tuberculose pulmonaire chronique, 25 (22.7%) avaient un test de Thorn abaissé.

2) Dix-neuf malades (23%) sur 81 devant subir une intervention pour tuberculose avaient un abaissement du test de Thorn.

3) Sur 19 malades dont le teste de Thorn était abaissé, et qui ont été opérés, 12 ont été l'objet de complications post-opératoires, probablement en relation avec la faiblesse de la réponse de leurs glandes surrénales.

4) Le test de Thorn semble être un des éléments pré-opératoires, qui associé aux autres investigations cliniques et biologiques, permet de mesurer l'aptitude à résister à l'opération, chez les malades atteints de tuberculose pulmonaire chronique.

5) Des études de l'éosinophilie après pneumonectomie, résection limitée, et thoracoplastie montrent que la faiblesse de la réponse des glandes surrénales est de même amplitude pour ces trois opérations.

6) Le deuxième temps de thoracoplastie produit un choc des glandes surrénales net et plus prolongé que pour la pneumonectomie, la résection pulmonaire limitée, ou le premier temps de thoracoplastie.

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## A Continuous Pneumo Apparatus

Hospital and Portable Models\*

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This paper deals with a newly-designed pneumo apparatus which incorporates the principle of a continuous and inexhaustible air reservoir for the introduction of a measured amount of air into the body cavity and features single valve control. It may be used for either *pneumothorax* or *pneumoperitoneum*.

Since the air reservoir is independent of the volume of the bottles, air for inflation is always available for immediate use in unlimited quantities without the necessity of periodically refilling the apparatus.

This new apparatus, therefore, is ideal for institutional or office use when many refills have to be given or when large quantities of air are administered, as in pneumoperitoneum. A portable model, incorporating the same continuous principle, is also available for treatment at the bedside or for home use.

This new apparatus retains all the desirable features of the familiar Cutler-Robinson<sup>1</sup> apparatus and adds many advantages. It employs the safest and most efficient of principles—that of gravity—for inflating the body cavity, yet the rate of flow can be hastened at will through the gentle use of a handbulb. Not only is it a safe instrument, sure and fool-proof, but also easy to understand and operate.

Essentially this apparatus (illustrated in Figure 1) consists of two inter-communicating chambers, a control valve, a water manometer, and a delivery assembly.

1) *The Intercommunicating Chambers:* Some important changes have been made in this system. As before, the chambers consist of two glass bottles (A and B) each of 2,000 cc. capacity graduated for direct reading into 50 cc. divisions and provided with a sliding pointer for determining the amount of air displaced. Each bottle is capped with a detachable metal top with two openings, one for air, the other for fluid. To the latter opening is attached a glass tube which extends almost to the bottom of the jar. Bottle A is fixed. Bottle B may be moved up and down on ratchet bars. One of the chambers is filled with air, the other with a colored watery solution of an antiseptic, such as 5 per cent phenol. Communication between the two chambers is brought about by means of a thick-walled rubber tube of sufficient length to permit chamber B to be raised above the level of the fixed chamber A when so desired.

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The pneumo apparatus, both hospital and portable models, was developed with the cooperation of George P. Pilling & Sons Company, whose contributions are gratefully acknowledged.

2) *The Control Valve:* A newly designed control valve of the interchange type operated by a lever and dial is used.<sup>2</sup> This single valve controls inflation, deflation, pressure readings, and complete closure and makes the apparatus of unlimited capacity.

Because the valve makes connection with either one of the chambers, a simple adjustment of the pointer on the dial changes the relation of the chambers to the delivery system. When one chamber is filled with fluid the other acts as an air reservoir and vice versa. After all the fluid has passed from one chamber to the other, the position of the pointer is merely changed to the chamber filled with air and the pneumo procedure continued with no interruption. The control valve, in other words, makes it possible for each chamber to serve in turn as an air reservoir and as a liquid reservoir. Compression of the hand bulb will hasten the passage of fluid from one chamber to the other.

A continuous and uninterrupted flow of air, therefore, independent of the capacity of the bottles, can be directed into the body cavity without the present necessity of first filling the apparatus or stopping the procedure during the operation to charge the apparatus. This is not only a great convenience and time saver but also makes for better technic.

Operation of the control valve consists merely of turning the pointer from one position to another on the dial. There are four different positions for the pointer, permitting three different communications and one neutral state (Figure 2). The position of the pointer on the dial is clearly indicated and easy to read. The positions are as follows:

- (1) N—Neutral. Valve completely closed.
- (2) M—Chest—Manometer.
- (3) A—Chest—Chamber A.
- (4) B—Chest—Chamber B.

3) *Corrected Water Manometer:* The usual U-tube water manometer is used. The intrapleural or intra-abdominal pressure is the difference in height between the levels of the water column in the two limbs of the manometer, expressed as centimeters of water. That is, the pressure within the pleural or abdominal cavity is capable of supporting a column of water as high as the number of centimeters difference between the two levels, or, is equivalent to the pressure exerted by a column of water of this height.<sup>3</sup>

Many operators are accustomed to using single-arm readings since the more commonly used types of apparatus are calibrated to read directly in centimeters. However, the single-arm reading unless corrected, that is, multiplied by two, is erroneous and makes for confusion. In the Cutler apparatus, the scale of the manometer is actually graduated in half centimeters but each half centimeter is numbered as though it were a full centimeter. In other words, the required correction is automatically made on the manometer scale. No further correction on the part of the operator is necessary. Pressure differences in centimeters of water are read directly from the scale, thus retaining all the advantages of single-arm readings.

The manometer is calibrated to record 24 centimeters of either positive or negative water pressure, which is sufficient for all purposes. Both arms

of the manometer are provided with traps to prevent ejection of water. The internal diameter of the tube is 4.5 mm. which is small enough to make the manometer sensitive and its excursion prompt and ample.

4) *The Delivery Assembly:* The delivery assembly (Figure 3) carries the air from the air reservoir into the body cavity. It consists of (a) long connecting tubing (which fastens to the outlet of the apparatus, (b) short connecting tubing (for connecting a and c), (c) three-way stopcock, (d) needle (2 inch, 20 gauge, short bevel), (e) 2 cc. syringe. Its use has been described elsewhere.<sup>4</sup> All connections, wherever possible, are of the Luer lock type for ease and security in operation.

#### *Use of the Continuous Pneumo Apparatus in Pneumothorax*

*Initial:* When performing an initial inflation with the Cutler pneumo apparatus, bottle B is elevated and the valve turned toward the manometer (M on dial) to bring it into communication with the pleural cavity. The bottle system is now completely shut off and no air can escape.

When the point of the pneumo needle (which is connected with the outlet on the pneumo apparatus by means of a three-way stopcock and rubber tubing) has entered the pleural cavity, in most instances negative pressure will be recorded on the manometer and the water column will oscillate with each respiratory effort. This indicates a free pleural space and the operator may now permit air to enter the pleural cavity.

The valve is now turned towards bottle A (marked A on dial). This automatically shuts off the manometer and brings the pleural cavity into communication with the air in bottle A. The water level in bottle B will gradually descend as water enters bottle A and gently displaces air into the pleural cavity, separating the pleural surfaces. The pressure under which this air enters the pleural cavity can be nicely regulated by varying the height of bottle B.

After 25 or 50 cc. of air has entered the pleural cavity the valve is again

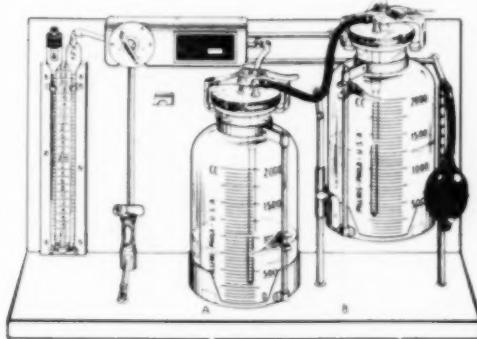


FIGURE 1

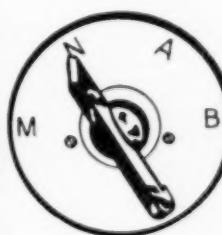


FIGURE 2

*Figure 1:* Author's Continuous Pneumo Apparatus (Hospital Model).

*Figure 2:* Lever and dial of newly designed control valve. This single valve controls inflation, deflation, pressure readings, and complete closure, and makes the apparatus of unlimited capacity.

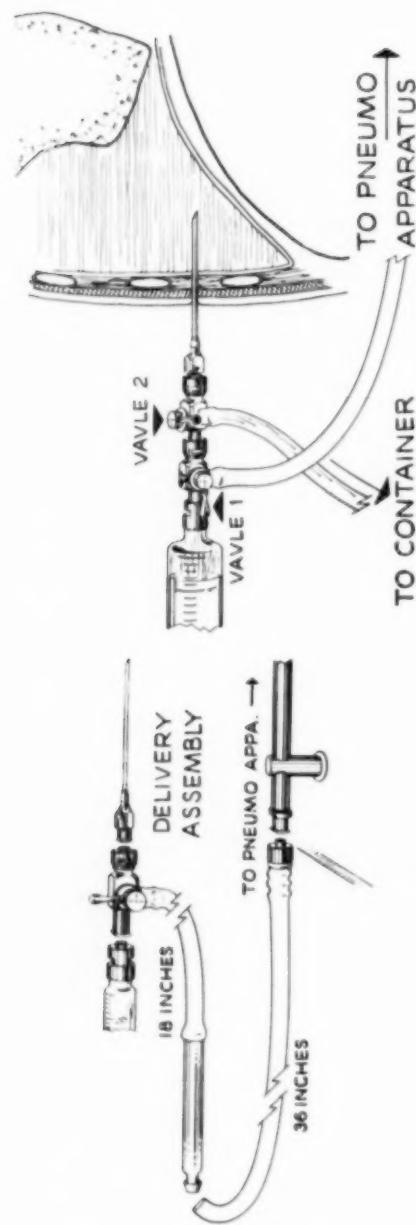


FIGURE 3  
FIGURE 4

Figure 3: Delivery assembly. The use of a valve between syringe and pneumo needle was first described by Rosenblatt in 1919.

Figure 4: Method of aspirating fluid of any type from the chest and replacing with air.

turned toward the manometer (M on dial) and the water bottle system is automatically shut off. No air now enters the pleural cavity and oscillations again appear on the manometer. This reassures the operator that the point of the needle is still in the pleural cavity. The valve is then turned back toward bottle A and more air is allowed to enter. This procedure is repeated after the introduction of every 25 or 50 cc. of air until 250 cc. has been administered. This completes the initial inflation.

Use of the pressure bulb is *not* recommended during an initial inflation.

*Refills:* Once the pleural surfaces have been definitely separated and an air space created, all subsequent inflations—known as “refills”—can be given without elevating bottle B. The intrapleural pressure is first taken on the water manometer. When oscillations are satisfactory and the pressure negative, air is allowed to enter the pleural cavity. Manometer readings are taken after each 50 or 100 cc. of air are given.

The pressure bulb attached to the inlet can now be used to advantage to hasten the rate at which the water displaces the air into the pleural cavity. When properly used it materially reduces the time required to inflate the pleural cavity. The rate of flow can vary from less than 100 cc. of air in one minute when hydrostatic pressure alone is used to more than 1,300 cc. per minute with the use of the hand bulb. The water system is thus always under the control of the operator. Air, however, should always be introduced gently and venely—never with speed or in spurts.

When the pressure bulb is used it is, of course, not necessary to have chamber B elevated since the compressed air above the water column becomes the driving force with which the water is evacuated, displacing air into the body cavity. The pressure bulb also makes possible positive pressure refills essential in extrapleural pneumothorax therapy.

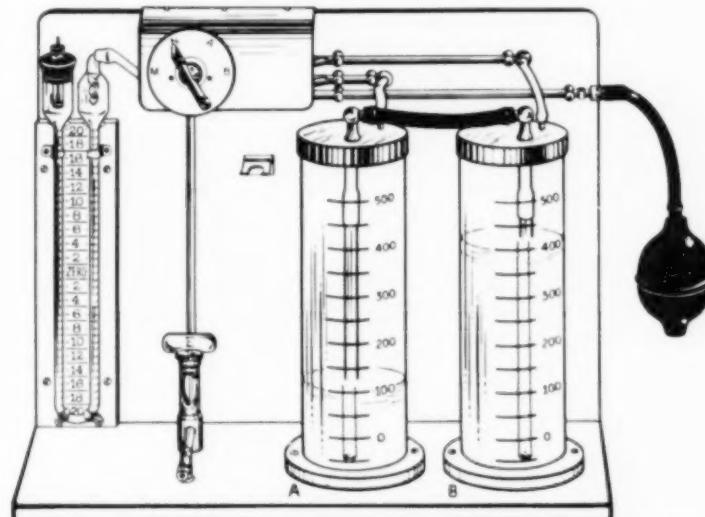


FIGURE 5: Author's Continuous Pneumo Apparatus (Portable Model).

When treating large numbers of patients it is more convenient and less subject to error to give as many refills as practical from the one chamber before switching to the other.

#### *Use of the Continuous Pneumo Apparatus in Pneumoperitoneum*

In pneumoperitoneum therapy the pneumo apparatus is used in exactly the same way as for pneumothorax. However, because of the positive pressure required to drive the air into the abdominal cavity, use of the pressure bulb is necessary at all times.

#### *To Withdraw Air Under Manometer Control*

The Cutler apparatus may also be used for the withdrawal of air from the pleural cavity when this is indicated. If bottle A is filled with water and bottle B is placed at a low level with the pointer set at A on the dial, water will flow from bottle A to bottle B creating a gentle suction. The air coming from the pleural cavity enters bottle A and occupies the area of the water displaced. A better method, however, is to use a syringe and needle connected with two three way stopcocks arranged in tandem and connected with the pneumo apparatus. Through proper adjustment of the stopcock valves, air can be aspirated from the body cavity and exhausted through the side arm of one of the stopcocks (valve No. 2 in Figure 4). Pressure readings can be obtained on the manometer at any time during the procedure. This method of withdrawal can be carried out with ease and simplicity of manipulation and has the further advantage of not exposing the body cavity to atmospheric air.

#### *To Withdraw Fluid with Air Replacement*

The use of two stopcocks in tandem as mentioned above can also be used advantageously for the removal of fluid, with air replacement, under manometric control (Figure 4). This method is more practical and has far more flexibility than is obtained with the four valves constructed for this purpose.

By changing the position of valve number 2, the fluid is forced into the tubing and into the container. As fluid is withdrawn, it can be replaced with air and pressure readings recorded through valve number 1, attached to the pneumo apparatus, after proper adjustment of the position of the valves. By this method one can empty the pleural cavity, wash it with various irrigating solutions, replace the fluid with air, introduce medication such as antibiotics and adjust the final pleural pressure without exposing the lumen of the needle to the atmospheric air and without any difficult manipulation.

#### *Portable Model*

Two models of the Cutler Continuous Pneumo Apparatus have been designed. One is for institutional use and for clinics where large numbers of patients have to be treated. The other is a portable type for use at the bedside or in the home (Figure 5). Both types operate on the same prin-

ciple and each has an unlimited air reservoir. The main difference is in the size of the bottles, 500 cc. volume instead of 2,000 cc. volume.

In the portable model both chambers are stationary and are made of plastic material. The heavy metal detachable lids have been replaced with a screw type cover. These features and the smaller size of the chambers have made possible a machine which weighs only 12½ pounds including the carrying case and fluid. Without the case the weight is a little over 7 pounds. The method of operation is the same in both models.

#### SUMMARY

A newly designed model of the familiar two-bottle Cutler-Robinson pneumo apparatus is described. The new model incorporates the principle of a continuous and unlimited air reservoir independent of the volume of the bottles and features single valve control.

Two models have been developed, one for institutional use and a portable model for treatment at the bedside or in the home.

#### RESUMEN

Se describe un nuevo modelo para neumotórax en base al aparato de dos frascos de Cutler-Robinson. El nuevo aparato incluye el principio del recipiente de aire continuo y sin limitación, independientemente del volumen de los frascos y tiene además, la característica de una sola llave de manejo.

Se han hecho dos modelos: uno, para instituciones y otro portátil para uso domiciliario.

#### RESUME

L'auteur décrit un nouveau modèle du vieil appareil à insufflations de Cutler-Robinson à deux récipients. Le nouveau modèle utilise de principe d'un réservoir d'air continu et illimité indépendant du volume des récipients, et comprend une seule valve de contrôle.

Deux modèles ont été construits, l'un pour l'usage courant, l'autre, portatif pour le traitement au chevet du malade ou à domicile.

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# Causes of Death in Carcinoma of the Lung in a Large Public Hospital

An Analysis of 186 Fatalities

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Carcinoma of the lung is not a cheerful disease at the present time. A physician who undertakes the analysis of a series of fatalities caused by it should therefore be prepared for what he may find. Because I have had my share of losses and have made my share of errors in this disease, I had thought that a review of 186 recent fatalities from Charity Hospital of Louisiana at New Orleans would hold few surprises for me. It held a great many. The concentration of medical and surgical errors and missed opportunities, combined with the fundamentally unfavorable circumstances which, in the light of our present knowledge, there seems no way at all of overcoming, has made this analysis one of the most depressing experiences of my professional life.

## *Basic Data*

The record library at Charity Hospital has on file for the period 1947-1951, 750 individual histories of carcinoma of the lung (Figure 1). Considerably less than half of these patients were considered suitable for exploration of the chest, considerably less than half of those explored could be submitted to either palliative or presumably curative pneumonectomy, and less than three-quarters of those submitted to pneumonectomy left the hospital alive. I have made no attempt to follow up these surviving pneumonectomized subjects, but my analysis of the 186 fatalities which occurred over this same period throws light upon what happened to some patients submitted to this operation. Twenty-two of the 33 patients who underwent pneumonectomy died during the immediate postoperative period. Eleven others, who survived the operation, later died in the hospital. Only four of the 11 lived for two years or more, and only one of these lived as long as five years.

Though I am not concerning myself in this review with the general incidence of carcinoma of the lung, a word might be said about its incidence at the New Orleans Charity Hospital. Between 1910 and 1927 no case of carcinoma of the lung or the bronchus is listed in the record library files. Only 21 cases are recorded from 1928 through June 1934. The first exploration for pulmonary malignancy at the hospital was performed in 1934 and the first pneumonectomy two years later. Since that time the number of cases has steadily increased. Between 1947 and 1951 the increase was more than 30 per cent, although the increase in hospital population over the

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same period was only 18.3 per cent. From the standpoint of the clinical surgeon, the debate over the incidence of carcinoma of the lung is merely academic. His problem is not the number of patients he is seeing, but how to see them earlier, while their disease is still operable.

The Charity Hospital figures bear out the overwhelming male predominance in this condition. Negro males, who furnished 69 per cent of the male hospital admissions for the 1947-1951 period, furnished over the same period 61 per cent of the cases and 64 per cent of the deaths from carcinoma of the lung. The concentration of negro patients at the New Orleans Charity Hospital, which is not equaled in any other institution of similar size in the country, gives these figures whatever importance they may possess.

The age incidence at Charity Hospital parallels that in most other series. The greatest concentration of cases was between 51 and 70 years, and the age range in the 186 fatal cases was from 37 to 88 years inclusive. Operation was not performed in any of the fatalities in patients under 40 years of age; as so often happens in malignant disease, cancer was apparently not suspected in these younger patients until it was too late to do anything about it.

#### *Factors of Mortality*

##### *The Mortality of Pneumonectomy:*

Over the past five years the hospital mortality for carcinoma of the lung treated by pneumonectomy has been 28 per cent. This is no higher than the mortality in certain other reported series, but it still requires explanation.

One obvious reason for it is the extension of indications for the operation to borderline cases and to patients who presented somewhat doubtful risks, even after preoperative preparation. All surgeons, I think, would agree that the lethal nature of this disease in the absence of radical resection fully warrants this policy in properly selected cases, which most of these fatal cases seem to have been.

Twenty-six of the 33 fatal pneumonectomies were palliative, which means that the risk was greater in them than it would have been in curative operations. In spite of the greater risk, however, palliative pneumonectomy is fully justified when it can be performed, if only on humanitarian grounds. Even if life is not greatly prolonged, the elimination of necrotic and infected tissues, foul exudation and sepsis makes the period of survival

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#### FIGURE 1

##### Summarized Data on Bronchogenic Carcinoma, Charity Hospital of Louisiana at New Orleans, 1947-1951.

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750 patients were admitted.  
Of these, 289 were explored.  
Of these, 125 were resected.  
Of these, 91 left the hospital alive.

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relatively comfortable, or actually useful and enjoyable. Churchill<sup>1</sup> is entirely correct when he says that it is not fair to term palliative pneumonectomy futile because it does not effect a lasting cure. Rather, as he emphasizes, the operation should be judged by the fact that "it makes the best terms possible with a disease that is already hopeless."

An analysis of the 750 cases by years is not reassuring. One might confidently have anticipated that with the passage of time the percentage of surgical explorations and of pneumonectomies would have increased and the mortality of resection would have decreased. That did happen, in general, in the period 1947-1950 (Figure 2). In 1951, however, the percentage of surgical cases was almost 10 per cent lower than in 1950, there was a small decrease in the number of pneumonectomies, and the hospital mor-

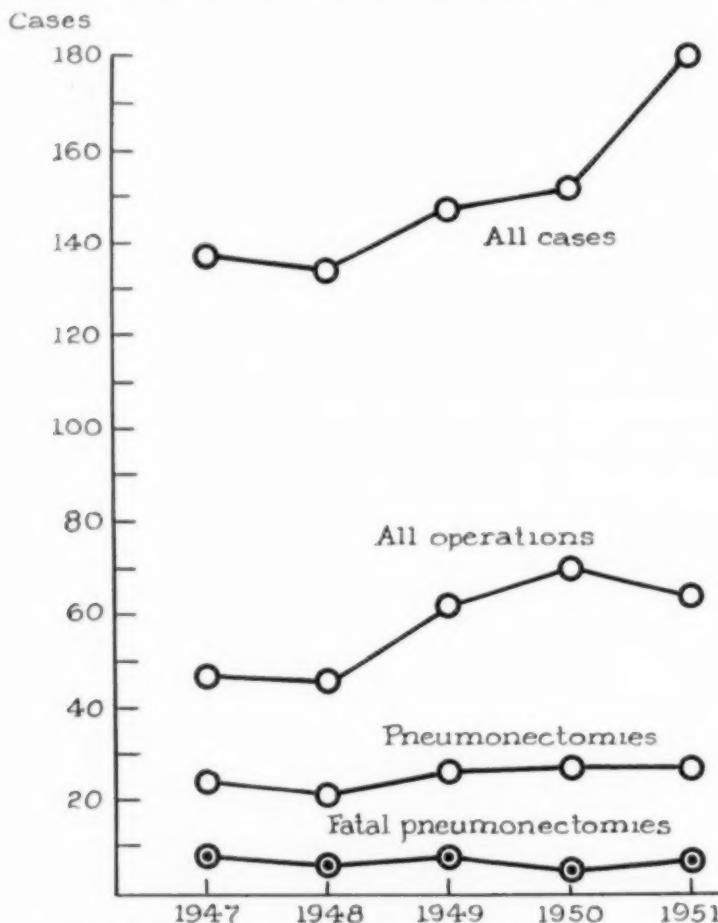


FIGURE 2: Yearly distribution of surgical cases, pneumonectomies and post-pneumonectomy deaths, 1947-1951.

tality for that operation rose by more than 7 per cent. The total number of cases treated in 1951 was only 180, which makes the figures in the various categories small and perhaps not really representative. Nonetheless, any backward step in carcinoma of the lung is not one which a surgeon can contemplate with equanimity.

The 22 postoperative deaths from pneumonectomy which occurred in this series of fatalities include five from causes which must always be deeply regretted, the mischances of operation and the technical errors which should not have occurred. All five deaths occurred in patients who presented good risks, whose growths were resectable, and who had no nodal or other extensions or metastases. Some of the operations were performed by surgeons with a wide experience in chest surgery. Others were performed by residents with limited experience, who were, however, operating under supervision. Pneumonectomy is a potentially dangerous operation, and, provided that the proper care and judgment have been exercised, there is nothing for the surgeon to do but to accept these mischances and accidents as part of its inevitable risk.

#### *Duration of Illness:*

Some of these fatalities illustrate again the unhappy and paradoxical fact that the shorter is the duration of symptoms, the shorter also is the duration of life after their onset (Figure 3). The details are even darker than the tabulated data indicate. In the 20 nonsurgical cases, for instance, in which the duration of symptoms before medical consultation was a

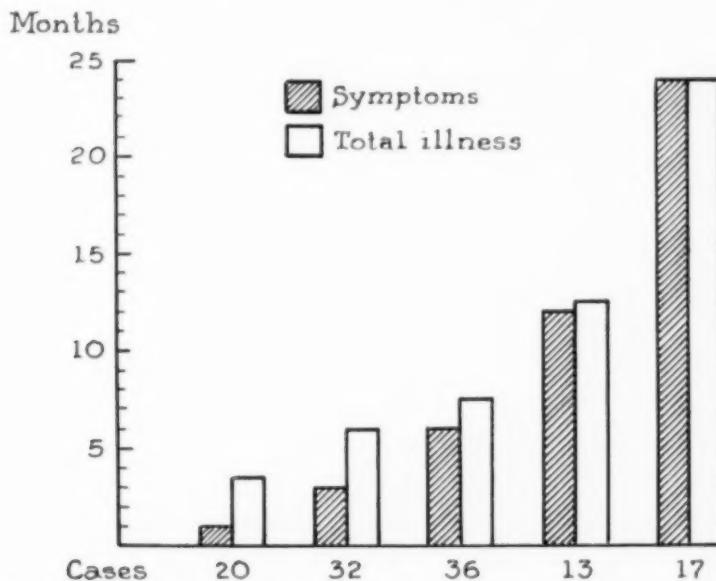


FIGURE 3: Duration of total illness in relation to duration of symptoms in 118 nonsurgical cases of bronchogenic carcinoma.

month or less, two patients lived for a year after they became clinically ill, but two others lived for only two weeks, three others for less than a month, and five others for less than two months.

The correlation between brevity of symptoms and of the total illness is also clear in many of the 23 patients submitted to exploration (Figure 4). It should be noted, however, that the duration of life in each chronologic category in this group is slightly longer than in the corresponding category in the nonsurgical group. It is worth emphasizing that, granting equality of risk, exploratory thoracotomy is not in itself a lethal procedure. As I shall stress later, one of the few practical methods of increasing the salvage in carcinoma of the lung in the light of our present knowledge is a prompter and far more universal resort to exploration of the chest.

About 40 per cent of the patients whose growths were considered inoperable or proved nonresectable had undifferentiated neoplasms. Only a few in this group lived longer than a year after they became aware of their illness and several of them died within a few weeks. Practically all of those who survived longest (a year or more) had epidermoid carcinoma or, in a few instances, adenocarcinoma. The four patients with anaplastic carcinoma who underwent pneumonectomy lived for an average of 5.4 months, against an average of 13.6 months for those with differentiated types of growths. Most patients with undifferentiated carcinoma of the lung are not candidates for surgery when they are first seen, and some authorities consider the mere identification of this cell type as, in itself, a contraindication to surgery.

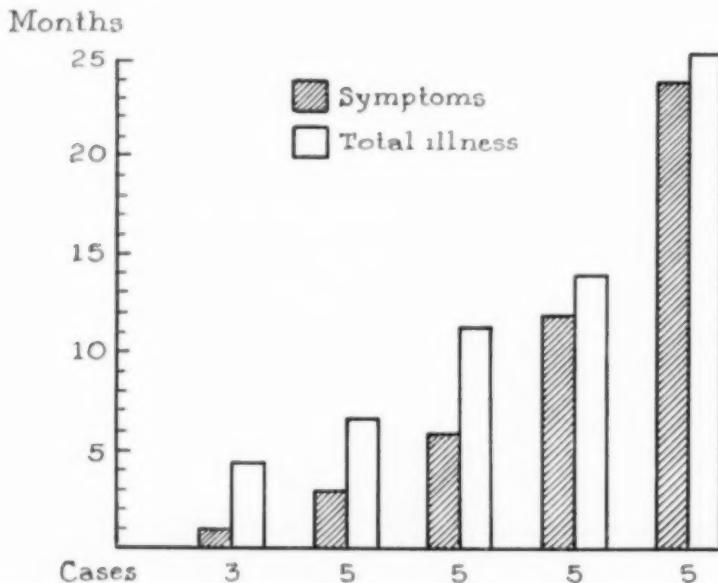


FIGURE 4: Duration of total illness in relation to duration of symptoms in 23 cases of bronchogenic carcinoma in which only exploration was possible.

*Extension and Metastases:*

These 186 fatalities illustrate again the extraordinarily wide extent and rapid development of extensions and metastases in carcinoma of the lung. In addition to the numerous instances of local spread to the regional and mediastinal lymph nodes, the pleura and the contralateral lung, there were 21 instances of metastases to the liver, 18 to the brain, 16 to the bones, 13 each to the adrenal glands and the heart and pericardium, 12 to the cervical lymph nodes, 11 to the aorta, seven to the superior vena cava, six to the supraclavicular nodes, four to the kidneys, three to the pancreas, and two each to the intestines and the thyroid. Actually, the spread of the disease must have been very much greater than these figures indicate, for they are based chiefly on the 73 cases in which autopsy was done and the 34 others in which exploration or pneumonectomy was performed. Exploration was necessarily incomplete in many of the surgical cases, while examination of the head was seldom permitted at postmortem examination.

*Diagnostic Errors and Delays*

From what has already been said, it is clear why the status of treated carcinoma of the lung is so often discouraging. Only when pneumonectomy can be carried out promptly—promptly in respect to pathologic process, not symptoms—are the results of treatment rewarding. Unfortunately, even when their duration of life is long enough to permit exploration and pneumonectomy, few patients are operated on promptly. Overholt and Schmidt,<sup>2</sup> who speak from a wide experience, have estimated that the average period of survival after medical consultation is 4.2 months when no treatment is instituted, 7.0 months with exploration, 9.6 months when pneumonectomy is performed in the presence of extensions to the regional lymph nodes, 10.0 months when there is gross evidence of extension, and 11.3 months when the growth is still local. They explain these depressing statistics by a still more depressing set: The average patient waits 3.8 months after the onset of symptoms to see his physician, undergoes his first roentgenologic examination 1.6 months later, and waits another 4.6 months for the diagnosis.

The figures for these 186 fatalities from the New Orleans Charity Hospital closely parallel Overholt and Schmidt's estimates. They show, just as does the experience of most other observers, delay by the patient, delay by the physician or physicians whom he first consults, and delay by the hospital which he finally enters.

Sixty-nine patients, 13 of whom were later submitted to pneumonectomy, consulted a physician, and sometimes two or three others, at longer or shorter periods of time after the onset of symptoms. Ten were promptly referred to Charity Hospital, in several instances with the diagnosis already made. The other 59 were admitted only after they had been treated for periods ranging from three weeks to two years. The majority were given cough medicine. Vitamins were prescribed liberally. Most of them received penicillin, with or without a sulfonamide. A few received all the antibiotics presently available. Some were treated for cardiac disease, which some of

them had also. A number, understandably, were treated for asthma, which they had had over long periods of time. A number were treated for tuberculosis, one of them in a sanatorium for five months, although in no instance does the diagnosis seem to have rested upon the demonstration of acid-fast bacilli in the sputum. One man was told that there was nothing the matter with him. Another, who complained of chest pain, was treated by local injections of novocaine.

Two patients deserve special mention. Both were told that they had chest tumors. Both were treated by deep x-ray. When one of them entered the hospital 10 months later, nothing could be done for him. The other, who was seen 12 months after he had been given 35 treatments, died four months after palliative pneumonectomy.

In 27 of these 59 cases, and in 53 others in which the patients applied directly to the clinics or the admitting room, diagnosis, treatment, or both were delayed in the hospital from two weeks to nine months. Many were treated symptomatically, just as many had been treated outside of the hospital. One was given emetine, in the belief that he had pulmonary extension of an amebic liver infection; he had neither. Several were treated for tuberculosis, in one instance for 259 days in the hospital before the correct diagnosis was suspected. Another was treated in the clinic for 18 months, during which time he was offered, and refused, thoracoplasty.

I do not mean to imply that it would have been possible to make a prompt diagnosis of carcinoma of the lung in all of these cases upon which I have been commenting, or in some instances to make it at all. In the 182 cases in which any sort of history could be secured, the story was completely typical in 55 and strongly suggestive, or suggestive to some degree, in 86 others; diagnosis was delayed, or missed entirely, in a number of these. In the remaining 41 cases, about 22 per cent of the total, the story was atypical and sometimes was so completely unrelated to the chest that only constant recollection of the insidious nature of carcinoma of the lung could have led to any suspicion at all that it might be present.

In a few cases the clinical picture of pulmonary malignancy was overshadowed by more urgent symptoms and signs. Three patients died of hemorrhage from the gastrointestinal tract, one of them after gastrectomy for duodenal ulcer. Another died after closure of a ruptured peptic ulcer, which was followed by evisceration. Still another died of mesenteric vascular occlusion. Two patients actually had pulmonary tuberculosis, in both instances advanced, and another also had primary carcinoma of the stomach. In two other fatalities the growth was an incidental finding at autopsy, though in both it had metastasized, in one instance to the adrenal glands.

Excluding these cases and some of the completely atypical cases, it seems fair to comment upon the complete absence of suspicion evident in numerous other cases treated both inside and outside of the hospital. Sometimes, too, the delay in instituting active treatment after the diagnosis was made is beyond explanation. In one case pneumonectomy was delayed for 10 months after bronchoscopy had revealed a granulating tumor. That

patient, inexplicably, lived for more than five years after operation, eventually dying from widespread metastases. In several cases in which the diagnosis was either positive or strongly positive, the patients slipped away from observation, only to return months later with inoperable disease or actually moribund. These patients do not include those who signed their own death warrants by delaying medical consultation too long. They also do not include two who refused pneumonectomy when it was offered to them. One of them accepted it two months later, but when the other returned, after 11 months delay and five bottles of hadacol, nothing at all could be done for him. Incidentally, the period of this study covers the period of violent advertising of that deplorable remedy, and more patients than the one just mentioned treated themselves with it, with equally disastrous results.

Several considerations in the management of the patients, both in and out of the hospital, deserve special comment:

1) Only a few roentgenograms were taken outside of the hospital, all of them, apparently, routine anteroposterior films. If they were negative, as they are likely to be early in the disease or in neoplasms in certain locations, that seems to have ended the matter. A number of patients who were investigated in the hospital with carcinoma of the lung in mind also had negative roentgenologic, bronchoscopic and cytologic reports, and that frequently ended the investigation in their cases too. The concept of thoracotomy as a diagnostic aid was overlooked altogether in many such cases in this series.

2) The promiscuous use of the antibiotics, and to a lesser extent of the sulfonamides, is apparently becoming a major problem in carcinoma of the lung. Waterman,<sup>3</sup> in a discussion of one of Overholt's<sup>4</sup> contributions, said that two of the greatest enemies of correct diagnosis in this disease are cough syrup and antibiotics, especially penicillin. This series of fatalities supports his opinion. Jones,<sup>5</sup> in discussing a paper by Paulson and Shaw<sup>6</sup> in 1948, said that there was then a longer delay in the diagnosis of this disease than there had been five years before, because five years before there had been only the sulfonamides to prescribe and in 1948 there was penicillin too. The result, he continued, especially if the patient went from one physician to another, was exposure to a great deal of therapy but very little diagnostic acumen. With the additional antibiotics available today, and the growing tendency to prescribe them casually and indiscriminately, the situation is even more serious now than it was when Jones called attention to it in 1948.

It is easy to see why these agents are prescribed, and why the error is so serious. The infections which are often a part of the pathologic process in carcinoma of the lung respond satisfactorily, and sometimes dramatically, to antibiotic therapy. The primary disease, as a consequence, is masked, and diagnosis is further delayed. I think it perfectly fair to say that in a number of these 186 fatalities the patients lost their lives because the symptomatic results of incorrect methods of treatment were so good.

3) Another consideration stands out in many of these 186 deaths. A large

number of the patients had been under intermittent observation in the clinics, and some under almost continuous observation, over periods of time when they must already have had carcinoma of the lung. Some of them were treated in the hospital. They were under treatment for cardiac disease, hypertension, skin, eye and orthopedic conditions. One underwent hernioplasty and two prostatectomy. One was under regular observation after a resection for carcinoma of the cecum. Re-reading of many of these histories brings to light stories which clearly pointed to trouble in the chest but which were ignored because of the concentration on other conditions. Two chest roentgenograms actually showed abnormal shadows, one in a patient hospitalized for cardiac disease. In all of these cases the pulmonary neoplasm developed while the patients were under direct medical observation. The opportunities for early diagnosis and treatment could not have been more favorable, but almost no use was made of them.

4) One particularly dangerous tendency in the management of these patients is also evident in a series of cases of carcinoma of the stomach which I have been studying from the New Orleans Charity Hospital over about the same period of time. I refer to the increasingly frequent habit of explaining symptoms on psychosomatic grounds. Many illnesses are, of course, entirely functional, and there is often some psychosomatic element even in organic diseases. But surely we are treading on very dangerous ground when our internes and residents, and even our medical students, reach for such explanations before they have excluded physical disease. I find it distinctly alarming that in at least 10 of these fatalities nervousness, hysteria, and other neuropsychiatric causes were advanced to explain symptoms, many of them clearly referable to the chest, before carcinoma of the lung was considered and excluded. These explanations were seriously advanced in three cases in which the patients were first seen 10, nine and eight days, respectively, before they died of this disease. One of them was refused admission to the hospital when she first applied; her diagnosis was hysteria, caused by the menopause and trouble with her mother-in-law. Neuropsychiatric elements and functional overlays were mentioned in several other cases. One patient was treated for conversion hysteria by reassurance therapy for six months before carcinoma of the lung was considered. Another was repeatedly referred to the neurologic clinic for psychiatric evaluation. The great good that neuropsychiatric medicine can accomplish will surely be destroyed if it is used in this dangerous and reckless manner.

5) Finally, it was disconcerting to observe how many times bronchogenic carcinoma was omitted from the list of diagnostic possibilities after the admission work-up. It would seem more reasonable to consider it, for instance, in a 71-year-old man with the complaint of cough, dyspnea, wheezing, voice changes and weight loss of 32 pounds over a three-month period than to list as possible diagnoses atypical thrombosis of the posterior inferior cerebellar artery versus a tumor of the posterior fossa. I suspect that one reason for the omission was that often the details of the history were merely recorded, not digested. Another reason may be that the phys-

ical examination in carcinoma of the lung is often negative and that the patient, as the recorders are accustomed to write, "does not look seriously ill." Of course, when a patient with malignant disease does look seriously ill his condition is usually hopeless. To exclude carcinoma of the lung because a man does not look as if he had it is, to quote an irritated British observer,<sup>7</sup> "ignorant, stupid, and almost contemptible."

#### *Diagnostic Considerations*

There was no lack of diagnostic investigation in most of these 186 cases. Roentgenologic examination was particularly rewarding. It is often stated that an x-ray shadow characteristic of cancer is never observed and the generalization is probably warranted. Nonetheless, in the 170 cases in this series in which roentgenograms of the chest were made, only seven were reported negative, and in 126 the radiologist stated that the condition was malignant or probably malignant. A less emphatic suspicion of malignant disease was raised in 16 other reports. In the remaining cases atelectasis, pleural effusion or abnormal densities called loudly for clarification and for exclusion of bronchogenic malignancy.

Fifty-eight of the 104 bronchoscopic examinations were diagnostic of carcinoma of the lung, chiefly because material for a satisfactory biopsy was thus obtained. In the remaining cases the examination was suggestive, inconclusive, or entirely negative. Direct visualization of the tumor was, as in most series, relatively infrequent. Bronchoscopy is a method which has not fulfilled its first promise in carcinoma of the lung, one reason being that most neoplasms are located where they cannot be visualized. There is small point to using this method in patients with obvious metastatic or terminal disease, and excellent reasons for not using it: Two patients in this series died almost immediately after it had been performed, apparently because they were too near the end of their journey to tolerate it.

The cytologic studies carried out in 79 cases, usually on bronchial secretions, were positive in 30 and suggestive in six others. This is an extremely useful method when the results are positive, particularly when they are positive on the first examination. A negative report, even when examinations are made serially, means nothing at all. Furthermore, to be of any value, every cytologic examination must be made by a thoroughly trained cytologist, who must be prepared to spend a great deal of time on each specimen. The usefulness of the method is greatly enhanced by the observation by Farber and his associates<sup>8</sup> that the sputum is equally as satisfactory for examination as the bronchial secretion. Examination of the sputum is 90 per cent accurate in their experience when as many as five specimens are studied. One questions, however, whether the patient's interests would not be better served by prompt exploratory thoracotomy in such cases. There seems considerable delay implicit in five cytologic examinations.

Only one patient in the Charity Hospital series was subjected to aspiration biopsy, a 75-year-old negro man, two months before he died. This is an unwise procedure in early cases of carcinoma of the lung, and an unneces-

sary one in advanced cases, in which no use can be made of the information even if the specimen is reported as cancer.

In a number of cases in this series the work-up was perfunctory and inadequate. It seems ungrateful, therefore, to complain that in a good many others there seemed far too much effort to establish an incontrovertible diagnosis. Roentgenograms, bronchoscopic examinations and cytologic studies were repeated again and again, with an apparent reluctance to accept what seems, in retrospect, clearcut evidence of pulmonary malignancy. In some cases, in fact, one received the impression that the perfectly conclusive results of the investigation were either not comprehended or not utilized. In other cases repetitious studies consumed time that might better have been spent hurrying the patient to the operating room.

The reverse of such excessive care was also apparent in this analysis, as has already been intimated. One diagnostic error, observed both in and out of the hospital, can be traced to the facile conclusion that if examinations and tests are negative, a disease can positively be excluded. Carcinoma of the lung certainly cannot be. Even in the face of negative roentgenologic and laboratory reports, a suspicious clinical history, if it is evaluated by a competent clinician, is ample reason for thoracotomy to establish or exclude the diagnosis. If this group of fatalities teaches anything at all, it is that suspicious lesions in the chest must be explored on suspicion alone, without delay for a time-consuming positive diagnosis. If the lesion is found to be a tuberculoma, a lung abscess, or a benign lesion, surgery is the procedure of choice. If the exploration is entirely negative, the surgeon may still feel that he has done what is best for the patient.

#### *Present Possibilities of Improvement in Diagnosis*

Perhaps the most tragic fact in the errors and delays which have just been discussed is that in the great majority of cases in this series they made little or no difference in the end results, at least so far as the hospital was concerned. Partly because of their own delay, but very often because of the insidious nature of their disease, nothing at all could be done for most of these patients when they were first seen. Only 33 were submitted to pneumonectomy, which was palliative in 26 cases. Only 22 others were explored. The symptoms which most of the patients presented when they were first seen—chest pain, hemoptysis, which was sometimes massive, wheezing, weakness, weight loss—indicated the advanced stage of their disease. Fourteen presented a typical superior vena cava syndrome. Ten had involvement of the vocal cords. In 14 cases headaches, disorientation, hallucinations and convulsions pointed to cerebral metastases. Craniotomy was performed in two of these cases and a trephining operation in another. In a number of cases dysphagia indicated involvement of the esophagus. Virchow's nodes, involvement of the cervical nodes, roentgenologic evidence of bone metastases, these and other observations all indicated the utter hopelessness of the disease in well over half of the patients when they were first seen in the hospital.

One indication of the stage of their disease is the brief time many of

them lived after they were registered in the clinics or admitted to the hospital. Some of them were actually moribund. Thirteen died within five minutes to 24 hours after admission. Sixteen others died within a week. Thirty-six others died within a month. In all, 89 of the 186 patients died within two months of the time they first applied to Charity Hospital for treatment. Only terminal care is possible in such cases as these.

One circumstance associated with many of these fatalities seems to invalidate the arguments of those who plead for government-controlled medicine on the ground that medical services are not available to much of the underprivileged population. A number of these 89 patients, as well as a considerable number of others who applied for treatment too late to be helped, had been regular attendants at the hospital clinics over long periods of time prior to this illness. Some of them can be described only as clinic habitués. They had been registered for years, in one instance for 20 years. They had been treated for innumerable ailments, some of them serious, some of them trivial. It testifies to the insidious nature of this disease, as well as to the tendency of patients to ignore symptoms until they become severe or incapacitating, that many of these men and women, with full knowledge of where medical care was available, simply failed to take advantage of the opportunity until the hour was so late.

Obviously, the problem in carcinoma of the lung is case findings and early diagnosis. Once the cases are found, therapy offers no problem, at least when pneumonectomy is still feasible and will probably be curative.

Ivy,<sup>9</sup> in listing possibilities of investigation and research in carcinoma of the stomach, wondered whether more attention should not be paid to serologic diagnosis. I think he put his finger upon our greatest need in carcinoma of the lung. I am convinced that the solution of the problem of both these diseases is the development of some biologic test which will do for them what the blood serologic test has done in syphilis and what the tuberculin test has done, somewhat less perfectly, in tuberculosis. I quite appreciate the importance of research along other lines, including a search for the causes of carcinoma of the lung, but I am nonetheless certain that until such a test does become available, early, curable cases will continue to elude us. When such a test has been devised we shall be confronted with the problem of persuading our patients to be tested by it, but at least we shall have a means of early identification of silent malignant disease which we do not now possess.

In the meantime, there are a number of other things which we can do to improve the situation in carcinoma of the lung. This series of 186 fatalities might have been very different if they had been done more often.

1) We can continue the campaign of public education, trying to get word to our private patients and to the lay public in general that any departure from the normal, including a persistent cough or repeated respiratory infections (one patient in this series had five attacks of pneumonia in 18 months), demands prompt investigation.

2) We must stop trying to relieve symptoms until we determine causes. This is not going to be easy. Patients who apply to us for relief of pain and

discomfort are going to resent it when relief is not the first order of business. They are also likely to resent it when they are not given penicillin or some other antibiotic. We shall have to speak very bluntly to them. We shall have to make it clear to them that they may lose their lives if their coughs are relieved or their upper respiratory infections are cured before the possibility of bronchogenic carcinoma is excluded.

3) We must put our own professional house in order. Chest physicians now know that carcinoma is perhaps the most frequent malignant disease in men, at least in middle and later life, and is far more frequent than virus pneumonia or, if such a condition exists, than unresolved pneumonia. Physicians who do not specialize in diseases of the chest either have not yet realized what has come to pass or, if they have, do not yet appreciate the potentialities of pneumonectomy when it is employed under optimal circumstances. It is seldom so employed at this time. In many of these histories I observed what other writers have also mentioned, a sort of reluctance on the part of physicians, even in the face of strong or actually conclusive evidence, to admit that the diagnosis in any given case was carcinoma of the lung.

We must teach the real facts of this disease to internes, residents and medical students. We must make them understand that this is an insidious disease, that it can exist with no symptoms at all, and that the symptoms to which it gives rise are not necessarily related to the chest. We must teach them that symptoms referable to the chest, even if they amount to no more than a persistent cough, require investigation, not symptomatic treatment. Finally, we must lose no chance to emphasize that the optimal time for surgery is the period of latency.

4) We must insist that a patient whose symptoms are not clarified by one method of diagnosis must be studied by another and must not be allowed to slip from observation until we can say positively that carcinoma of the lung is not present.

5) We must, however, also take the position that diagnosis in any suspected case of bronchogenic carcinoma is a matter of extreme urgency, as urgent, comparably, as is diagnosis in an acute abdominal emergency. In the review of these fatalities from the New Orleans Charity Hospital I was impressed with, as well as depressed by, the leisurely pace of the investigative routine and the inertia that so often failed to surmount the niceties of clinic red tape and hospital protocol. We must teach and preach that this is a disease of relentless progression, in which there is no time for repeated re-examinations and the "return in two weeks" method of investigation. A loss of weeks, or even of days, may conceivably mean the difference between life and death. In this disease who can say when a bloodborne metastasis or a regional extension may vitiate the effect of the pneumonectomy planned for next week or even for tomorrow? As Overholt<sup>4</sup> has put it, the study of carcinoma of the lung must be geared to the cancer potential, with the surgical amphitheater regarded as the highest court of appeal. As matters stand now, prompt diagnosis, with exploratory thoracotomy regarded as an integral part of the diagnostic

routine, is the best that we can do in this disease. At the present time we are not doing our best, nor shall we be doing it until we resort to exploration far more often on mere suspicion, or on the basis that it is impossible to say that bronchogenic carcinoma is not present.

5) We are making scarcely any use at all of one method of case finding which is readily available to us, utilization of the data secured in mass chest surveys. The special effort made along these lines in the survey conducted in Boston in 1949 turned up 43 primary carcinomas of the lung, 20 of them resectable.<sup>10</sup> Last year, with no provision for special screening, 16 films taken in the mass chest survey in New Orleans showed shadows regarded as suspicious.<sup>11</sup> An analysis of these cases is instructive: Eight patients are at present under investigation. One has been lost from observation. One consulted his private physician. One exploratory thoracotomy revealed a tuberculoma, which was removed. The five remaining patients were hospitalized at the New Orleans Charity Hospital, where one promptly died, of bronchogenic carcinoma complicated by a bronchopleural fistula. Another was explored and found to have inoperable disease. But the three other patients have undergone resections which there is reason to believe may be curative.

This is a small harvest, it is true, 43 cases in 537,012 examinations in Boston, five proved cases, at least to date, in 50,624 examinations in New Orleans. In both cities some of the fruit has been bitter indeed. These observations, however, open up a new and hopeful field of investigation. If the various organizations and government agencies concerned with cancer can combine their forces with those concerned with tuberculosis, more cases of silent, resectable carcinomas of the lung will be found than, in the present state of our knowledge, can be found by any other means.

As I said in the beginning of this paper, carcinoma of the lung is not a cheerful disease. Most thoracic surgeons will agree with me. In 1937 I prepared to perform my own first pneumonectomy, after a great many rehearsals on cadavers and dogs, with the confident expectation that I was dealing with early, operable disease in a good risk patient. The man was a good risk but his disease was inoperable. I have entered many other chests since then with the same high expectations, only to find the same hopeless situation. On the other hand, I can remember other patients who have survived pneumonectomy for five and seven and 10 years, and who are still well.

Graham's first surviving pneumonectomized patient, operated on in 1933 and still alive and well 18 years later, appears in most papers on bronchogenic carcinoma. He should. As Churchill<sup>1</sup> says, the chest surgeon who is tempted to despair would do better to remember him than to draw any conclusions at all from the preliminary analyses of data on carcinoma of the lung now recorded in the literature.

#### SUMMARY

A distressing picture emerges from the analysis of 186 fatalities from carcinoma of the lung at Charity Hospital of Louisiana at New Orleans.

Patients often delayed seeking treatment. Private physicians and hospital staff often failed to suspect the diagnosis or were slow to recommend surgery. The investigation was sometimes perfunctory, sometimes unnecessarily repetitious, and sometimes enmeshed in hospital routine and protocol. Appallingly often the clinical course was far too brief to permit any positive action. If the mortality is to be lowered in this disease, which is now of major importance among malignant diseases, the profession must (1) develop a far higher index of suspicion concerning it; (2) explore the chest on suspicion much oftener; (3) stress the urgency of diagnosis and treatment; (4) investigate the whole man rather than limited fields whenever adults seek medical care for any reason whatsoever; and (5) make the fullest possible use of data available in mass chest surveys.

#### RESUMEN

Del análisis de 186 defunciones por cancer del pulmón en el Charity Hospital de Louisiana, en Nueva Orleans, resulta un cuadro desalentador. A menudo los enfermos buscaron el tratamiento con demora. Los médicos particulares y el personal de hospital frecuentemente no sospecharon el diagnóstico o fueron morosos para recomendar la cirugía. La investigación fué a veces superficial, a veces innecesariamente redundante, y en otras ocasiones enredada en la rutina y la documentación del hospital. Es sorprendente ver que con frecuencia la evolución clínica fué demasiado breve para permitir una intervención activa. Si se ha de lograr bajar la mortalidad por esta enfermedad, que ahora es de la mayor importancia entre las malignas, los médicos deben: (1) estar alerta para sospecharla; (2) explorar el torax mas a menudo, al sospecharse la enfermedad; (3) reclamar la urgencia de diagnóstico y tratamiento; (4) examinar todo el organismo cuando un adulto busca atención médica por cualquier causa, y (5) aprovechar tanto como sea posible los datos que las investigaciones en masas proporcionan.

#### RESUME

Une analyse de 186 décès par cancer du poumon faite à l'Hôpital de la Charité de la Louisiane (New-Orléans) dessine un tableau alarmant. Souvent les malades ont trop attendu avant de se faire traiter. Les médecins de clientèle privée et les médecins des hôpitaux ont souvent méconnu le diagnostic ou ont trop tardé à recommander l'acte chirurgical. L'examen du malade fut parfois trop léger, parfois des recherches furent répétées sans nécessité et parfois accaparées par la tradition et la routine hospitalière. D'une façon affreusement fréquente, l'évolution clinique fut trop rapide pour permettre aucune action efficace. Si l'on veut abaisser la mortalité de cette maladie qui est maintenant de la plus grande importance parmi les affections malignes, il faut: (1) Faire en sorte qu'elle soit beaucoup plus facilement suspectée; (2) faire beaucoup plus souvent une exploration du thorax quand on la redoute; (3) insister sur le caractère urgent du diagnostic et du traitement; (4) faire un examen complet plutôt que des investigations partielles chaque fois qu'un adulte vient consulter un

médecin pour une raison quelconque; (5) se servir au maximum des données de l'examen systématique du thorax dans les collectivités.

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## An Improved Cardiac Defibrillator

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In view of the recent interest in cardiac arrest and ventricular fibrillation it seemed surprising, some months ago, to find no carefully-designed defibrillator was commercially available in the market. Those interested in the problem were using home-made or locally manufactured equipment not generally available. Although commercially available defibrillators have since been placed on the market, I wish to describe an instrument of improved design developed in conjunction with the Coleman Instrument Company. The basic electrical system is based on that described by Stover<sup>1</sup> and Birnbaum.<sup>2</sup>

The following specifications were laid down, and successfully incorporated in the design of the instrument:

- 1) The defibrillator shall deliver a 60 cycle output of intensity adjustable between 0.5 and 2.5 amperes.
- 2) This output should be in the form of a pulse of adjustable length, automatically timed within the instrument. The pulse length interval should be adjustable between 0.03 seconds and 0.50 seconds by a calibrated control on the panel.
- 3) The pulse network should be so designed as to render impossible overtreatment of the patient through a personal error of the operator.
- 4) The entire instrument should be so designed that in the event of failure of any of its parts, such failure would be harmless to the surgeon and the patient.
- 5) The output of the defibrillator shall have no detectable electrical potential with respect to earth ground, i.e., it should be impossible for the surgeon to receive a shock while simultaneously touching an electrode and a grounded object during treatment.
- 6) A test circuit should be incorporated in the instrument to show that all is in order before its application to a patient. The test should include proof that the proper current intensity will be delivered to the patient's heart, and should also prove electrical continuity at the electrodes. These two tests should be made automatically by pressing a "Test" button, and yet should not under any circumstances strike an arc at the electrodes. Such an arc could conceivably touch off a disastrous explosion in a cyclopropane atmosphere.
- 7) The operation of the instrument should be simple in the extreme, so that a previously unpracticed operator can successfully carry through a treatment.
- 8) The electrodes employed should be easily sterilized, and so designed as to minimize shock hazard to the user.

The current output to the electrodes is derived from a 250 v.a. 110v, 60

cycle isolating transformer, and is fed to the electrodes through an adjustable current limiting resistor variable between 50 and 250 ohms. This restricts the maximum current obtainable to 2.5 amperes.

The output current is pulsed by a relay whose coil constitutes the plate load of a type 2050 thyratron tube. In the input grid circuit of this tube is a time delay network whose DC negative charging bias is supplied by a selenium rectifier power supply. When the "Treat" button is pressed, the thyratron conducts, and the pulse relay actuates. Simultaneously, a negative charging voltage begins to build up on a condenser across the input grid. As soon as this negative voltage equals -2 volts, the thyratron extinguishes, and the pulse relay drops out. So long as the "Treat" button is held down, the tube will be held nonconductive by this applied negative bias which slowly increases until it equals -10 volts. When the "Treat" button is released, this accumulated charge is returned to set ground and



The Coleman Defibrillator.

the operation may be recycled at will. Proper selection of the values of charging bias voltage, condenser capacity, and charging resistance gives the desired time interval of pulse duration. Thus timing of the current impulse length is rendered independent of human error, and is consistently reproducible within accuracy limits of plus or minus 1/120 of a second.

"Fail Safe" operation of this instrument was considered of major importance, since a human life is always dependent upon its proper operation. While the likelihood of failure is small, four preventive steps were taken to assure positive operation, and prohibit dangerous failure. In series with the DC bleeder network of the selenium rectifier power supply is included the coil of a DC relay. This relay must actuate before the rest of the circuit will operate. In the event of bias supply failure, this relay will not operate, and the instrument becomes inoperative. The other relays in the circuit are so positioned physically that breakage of an armature spring, or coil failure will prevent the function of that relay. The electrode leads at all times are internally shorted together except when the "Treat" or "Test" buttons are pressed. This prevents any insulation leakage from developing an electrical potential across the electrodes. The entire instrument is internally fused at 5 amperes, thus preventing damage in the event of an accidental short circuit.

Since the electrodes derive their current from the secondary winding of an isolation transformer, it is impossible for the surgeon to be shocked by coming into accidental contact with a grounded object such as a wet concrete floor, or a metal table frame.

Pressing the "Test" button performs two operations simultaneously. It passes the output of the isolation transformer directly through the adjustable limiting resistor and the AC ammeter on the panel. By rotating the "Current Control" knob while the "Test" button is depressed, the operator can set the delivered current to any previously selected value within the range of 0.5 to 2.5 amperes. Pressing the "Test" button also turns on the "Test" pilot light, and connects the electrode wires across this light. Touching the electrode plates together shorts out the light, extinguishing it, and proving that there is electrical continuity to the electrode plates. Since the NE-51 pilot light only draws 1/25 watts of power, no arc can be formed by touching the plates together. The voltage appearing at the plates during this test operation is small and harmless.

Operation of the instrument, because of the various safety circuits and automatic action, becomes feasible for the untrained operator. Since the defibrillator will warm up ready for use within 20 seconds, it is not necessary to leave the power on at all times during surgery, thus extending its operating life indefinitely. The operating instructions are clearly printed inside the lid of the instrument and can be quickly understood. They read as follows:

- 1) Plug line cord into 110 volt AC source.
- 2) Turn on main power switch and allow 1/2 minute warmup time.
- 3) Provide the surgeon with two sterile electrodes, and plug the electrode wires into their handles.

- 4) Press the "Test" button. Adjust "Current Control" knob and "Current Range" switch to obtain meter reading suggested by surgeon. Have surgeon touch the electrode plates together momentarily, which should extinguish the "Test" light. Release the "Test" button.
- 5) Set the "Pulse Length" control to the interval requested by the surgeon.
- 6) Before the surgeon applies the electrodes to the heart, press the "Treat" button and observe that the "Treat" light blinks once and then is dark.
- 7) Instruct the surgeon to apply the electrodes, and await his order to "Treat".
- 8) At the order, press the "Treat" button firmly once, and release. Be ready to repeat this if so ordered.

The electrodes are made of brass and copper, polish nickel plated, with white nylon insulating handles. They may be autoclaved or sterilized in the same manner as other instruments without special consideration.

This instrument has been successfully used in arresting ventricular fibrillation in the dog. Anaesthesia was produced by intravenous nembutal and the chest and pericardium opened. The animal was allowed to breathe benzol fumes until the blood pressure dropped, when the benzol was discontinued and epinephrine 0.02 mgm. per kilo, injected intravenously. This produced a marked ventricular fibrillation, which was immediately arrested by three consecutive shocks of one-half ampere at 1/10th of a second. After the heart had recovered, a second fibrillation was induced in the same manner and again successfully broken with the defibrillator. Heart action could not thereafter be restored, however, probably due to an overdose of benzol.

*Acknowledgment:* The design and manufacture of this instrument were under the direction of H. J. Whitehill, Jr., Chief, Electronics Section, Coleman Instrument Company.

#### SUMMARY

An improved cardiac defibrillator and its successful use on the dog has been described.

#### RESUMEN

Se describe un desfibrilador mejorado y su éxito satisfactorio en el perro.

#### RESUME

Les auteurs décrivent un défibrillateur cardiaque perfectionné et son utilisation satisfaisante sur un chien.

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## Congenital Multiple Cysts of the Lung

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This paper is concerned with congenital multiple cysts of the lungs. The relevant cases were discovered when examining immigrants in the reception camps by means of mass radiography. The method was applied with the aim of detecting tuberculosis among the newcomers. Unexpectedly we found an exceedingly high incidence of different kinds of cysts.

Examining the immigrants to Israel we found within a period of approximately one year 188 cases of cysts of different kinds. Among these 92 showed the particular form of congenital multiple cysts.

Of the 92 affected persons 62 were male and 30 female, thus the incidence of the disease among men was more than twice as high as among women.

As to frequency in the different age-groups one should note, that children below eight years of age were not examined (for technical reasons only). The disease was most frequently seen among young persons.

Most of the cases (80) were discovered in the years 1950-51, when the immigrants came mostly from Arab countries. Ten immigrated in the years 1947-1949 and two others (Arabs) were Israel born.

Only nine were of European origin, and it is interesting to note, that in these cases it was difficult to determine whether we were dealing with cystic disease of the lung or with cystic bronchiectases.

Spontaneous complaints about any symptom were not heard. In 24 cases we could not find out whether symptoms had previously been noted. As far as we succeeded to get our questions answered, the information was as follows: 30 reported no previous symptom. Thirty-eight complained mostly of cough. In 26 cases the cough was associated with purulent, bad-smelling sputum. Three had had haemorrhages. Toxic signs, such as fever and weakness, were found in five. In the 38 cases, which had clinical symptoms, the sedimentation rate was variably high. The blood picture revealed no essential change. The bacteriological tests, including cultures, of the sputum and of the gastric contents were negative for tubercle bacilli.

Roentgenographic picture of the disease appeared as a set of circular shadows with thin contours, sometimes of approximately equal, sometimes of different diameters. In the majority of cases the shadows covered a whole lobe, less frequently a single segment or two lobes. Affection of three lobes was rare. In the great majority of cases no sign of inflammation in the tissue, surrounding these air-balloons could be found.

On the basis of our observations it can be said, that the right and the left lungs were affected almost in equal measure. In 16 cases the shadows covered two lobes, in one case three lobes were affected. In 75 cases the pathologic changes were localized in one lobe only: 30 in the upper lobe; 18 in the middle lobe or lingula; 27 in the lower lobe.

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In 17 cases the circular shadows were spread throughout more than one lobe. In eight the left lung was affected in its entirety. In five the localization was in the lingula and in the right middle lobe, in three in the right middle and lower lobes and in one in the right middle and upper lobes and in the lingula.

Infection may roentgenographically change the whole picture to such an extent, that the basis of the disease, the cystic pattern, becomes blurred and less characteristic. The radiographic examination should, of course, include a lateral and an oblique roentgenogram in addition to the routine roentgenogram. Moreover, we have, with the help of tomography, succeeded in determining the particular structure of a lung affected by cysts. The importance of bronchography should not be overlooked in completing the roentgenographic examinations. Bronchoscopy is also carried out, though its diagnostic value for the cases under consideration is small.

We have tried to find whether there is any connection between the clinical symptoms on the one hand and the age of the patient and the localization of the finding on the other hand. It seems that symptoms are more frequent in the young. As to the connection between the localization of the disease and the clinical symptoms, we have noted the following:

Among 30 with localization in the upper lobe: 7 complained of symp-

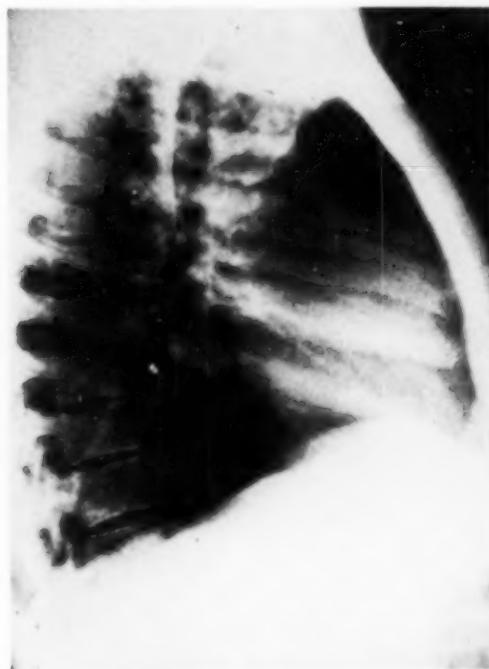


FIGURE 1, Case 1 (lateral roentgenogram).  
Circular shadows in the apical segment of the right upper lobe.

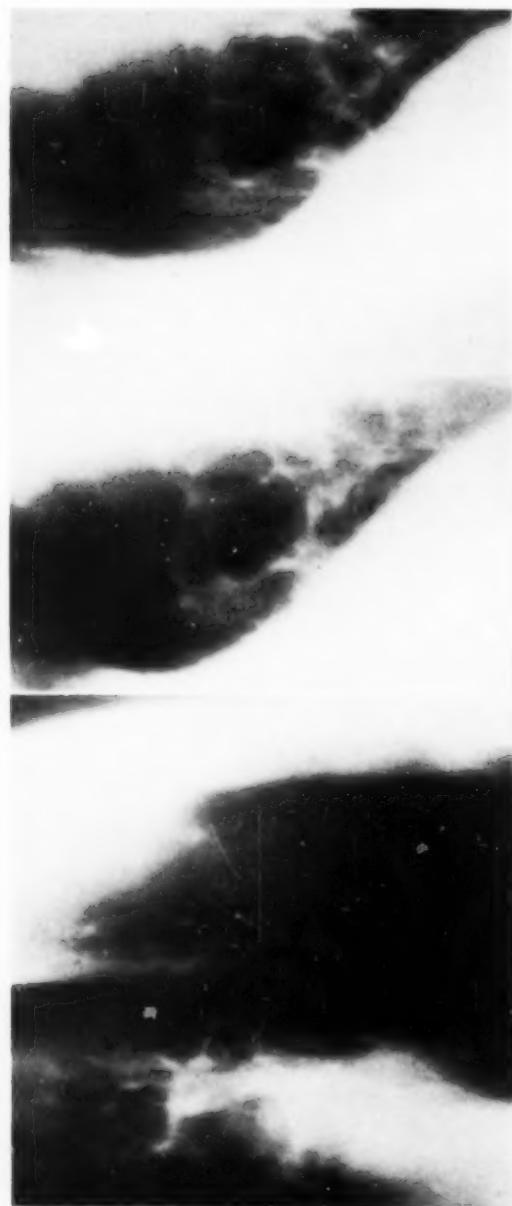


FIGURE 2

Figure 2, Case 3 (lateral tomogram, layer 7). Cysts in the lingula.  
Figure 3, Case 3 (AP-tomogram, layer 14-15). Cysts in the lingula.

FIGURE 3

toms, 14 did not, 9 unknown. Among 18 with localization in the middle lobe: 7 complained of symptoms, 7 did not, 4 unknown. Among 27 with localization in the lower lobe: 14 complained of symptoms, 8 did not, 5 unknown.

This may be explained by the drainage being more efficient in the upper

TABLE I  
CONGENITAL MULTIPLE CYSTS OF THE LUNGS

Number of cases: 92							
	Male: 62						
	Female: 30						
<i>Age:</i>							
up to:	20	30	40	50	60	70	above 70
cases	29	17	10	14	10	6	6
<i>Years of immigration:</i>							
1947-1949	1950		1951		Israel born		
	10	32		48	2 (Arabs)		
<i>Countries of origin:</i>							
Arab Countries					European Countries		
Iraq	53				Roumania	7	
Iran	11				Poland	2	
Yemen	8						
Tripoli	4						
Morocco	3						
Syria	1						
Turkey	1						
<i>Localization:</i>							
Left side	44						
Right side	42				(both sides 6)		
<i>One lobe:</i> 75							
Upper lobe		Total		With Symptoms	Without Symptoms		Unknown
Middle lobe or lingula		30		7	14		9
Lower lobe		18		7	7		4
		27		14	8		5
<i>Two or three lobes:</i> 17		Total					
Upper and lower lobe		8					
Middle lobe and lingula		5					
Middle and lower lobe		3					
Upper and middle lobe lingula		1					
Cases with symptoms		38					
Cases without symptoms		30					
Unknown		24					
Cough		32					
Sputum		26					
Hemorrhage		3					
Fever		3					
Weakness		3					

than in the lower lobes, which makes the chances for a secondary infection in the former much smaller.

Among our patients there were eight in whom the cyst occupied the whole left lung. In all of them clear signs of atelectasis were found. The mediastinum was shifted to the left, the retrosternal space was enlarged, a mediastinal hernia characterized the picture. This finding, common to these eight cases, and not to be found in instances where a lobe was involved only partially, suggests the hypothesis of an embryonal anomaly



FIGURE 4



FIGURE 5

*Figure 4, Case 4 (routine roentgenogram). Cysts in the left lower lobe.  
Figure 5, Case 4 (lateral roentgenogram). Cysts in the left lower lobe.*



FIGURE 6

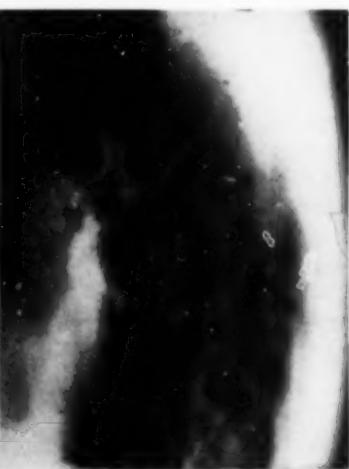


FIGURE 7

*Figure 6, Case 4 (AP-tomogram, layer 5). Cysts in the left lower lobe.  
Figure 7, Case 4 (lateral tomogram, layer 8). Cysts in the left lower lobe.*

in the bronchial system. The following considerations support the congenital origin of cysts in our cases:

- a) The greatest number of patients with the finding of multiple cysts belong to the younger age groups.
- b) In the routine mass examinations we found many cases with no signs of secondary infection.
- c) In the case histories we found no indication for supposing a pathologic process in the past, which might have caused the present finding.
- d) In routine examinations of several hundreds of thousands of immi-



FIGURE 8. Case 6 (routine roentgenogram).  
Cysts in the right upper and middle lobes and in the lingula.



FIGURE 9

FIGURE 10

Figure 9, Case 7 (routine roentgenogram). Cysts in the whole left lung.  
Figure 10, Case 7 (lateral tomogram, layer 7). Cysts in the whole left lung.

grants during some years we found cases with multiple cysts previously among the new-comers from the Yemen, and more recently among those from Iraq. As the phenomenon is rarely to be found elsewhere in the world and remarkably frequent among certain communities, it may be of hereditary origin.

One has to bear in mind whether any other disease, not congenital, may have a clinical and x-ray appearance similar to that under discussion. Sometimes dilatation of bronchi shows a cystic form, though the usual appearance is cylindric or saccular. But even if there is a resemblance in appearance, the findings differ as follows:

1) Signs of inflammation in the surrounding tissue characterize bronchiectasis and are absent in multiple cysts.

2) Bronchiectasis is mostly localized in the lower lobes, whereas congenital multiple cysts may affect any part of the lungs, i.e. the lower and upper lobes alike. Considering our data, the right upper lobe is the most frequently affected.

In discussing the differential diagnosis between congenital multiple cysts and bronchiectasis the results of clinical and x-ray examinations are of decisive significance. The importance of additional anatomo-pathological investigations might be stressed. Our present study is to be completed by such research.

Results of histopathologic examinations were published by Dickson, Clagett and McDonald. The microscopic examinations confirm our point of view: In cases of bronchiectatic cysts inflammatory changes were found in the tissue of the lung, whereas congenital cysts were generally surrounded by healthy tissue. The neighboring tissue was seldom affected, but if so, very slightly.

In addition, there was quite a remarkable histologic finding: Bronchial epithelium was covering the bronchiectatic cysts and the congenital as well. The walls were even composed of the same material as the walls of the bronchus, i.e. cartilage, smooth muscle, elastic tissue, lymph nodes. However, whereas in the case of dilatation of the bronchus the structure of the bronchial wall is preserved, in congenital cysts these same elements appear, but in a disordered and different arrangement.

The comparison between the findings in our cases and those published by Hyde in 1951 and also earlier by Oswald, Neville and Parkinson shows that "Cystic disease" is not a definite entity but it includes a number of different forms, which must be discussed separately.

The findings described by the above mentioned authors were as follows: small cysts with thin walls spread throughout the whole of both lungs. Anatomic examination revealed fibrotic changes in the whole of the interstitium. The patients are mostly males (as in our cases). There are characteristic clinical symptoms: Frequent spontaneous pneumothorax, unilateral or bilateral; progressive shortness of breath; increasing heart lesion on the right side, the latter often being the cause of death. Hyde calls the disease "bilateral fibrocystic disease of the lung," which is one kind of a cystic disease. The congenital multiple cysts, as described by us,

are of a quite different kind, both with regard to symptomatology and prognosis.

Their clinical symptoms are due not to the cysts themselves, but to secondary infection. The danger of infection is imminent in each case, but it would be an exaggeration to predict, as Graham did, that infection is inevitable. We have seen people who reached old age free from secondary infection.

As far as therapy is concerned, we see but one way: the excision of the affected lobe (antibiotic treatment has only symptomatic value). We should, however, be wary of extreme attitudes. Each case should be judged on its own merits. In the case of an aged person with clinical signs of infection it is worth while trying conservative treatment with penicillin or other antibiotics. If symptoms of infection are noted in a young person, we shall not hesitate to recommend surgery.

#### SUMMARY

In mass examinations of immigrants, who mostly came from Arab countries in the years 1950-51, an unprecedented large number of cases (188) of pulmonary cysts was detected. Out of these 96 were with large single cysts (mainly echinococcus) and 92 with congenital multiple cysts, occupying one or more lobes. A clinical and roentgenologic picture of the disease is given, the congenital origin of the disease is discussed.

The differential diagnosis between this disease and bronchiectatic cysts is based on clinical and roentgenological evidence, which corroborates the histopathological findings, published in the literature. The importance of a precise determination of the different varieties of pulmonary cysts is emphasized. The disease rarely manifests itself by symptoms; the latter may appear when the disease is associated with secondary infection.

#### RESUMEN

En el examen en masa de inmigrantes, la mayor parte provenientes de los países árabes, en los años 1950-51, un gran número sin precedente de casos (188) de quistes pulmonares fué encontrado. De ellos 96 tenían grandes quistes simples (principalmente equinococcicos) y 92 quistes congénitos múltiples ocupando uno o más lóbulos. Se da una descripción clínica y roentgenológica de la enfermedad y se discute el origen congénito de la misma.

El diagnóstico diferencial entre esta enfermedad y los quistes bronquiectásicos está basado en evidencia clínica y roentgenológica que corrobora los descubrimientos histopatológicos publicados en la literatura. La importancia de la determinación precisa de las diferentes variedades de quistes pulmonares es remarcada. La enfermedad rara vez se manifiesta por síntomas; éstos pueden aparecer cuando la enfermedad está asociada con infección secundaria.

#### RESUME

Les examens systématiques d'immigrants venant pour la plupart des Pays Arabes dans les années 1950 et 1951 montrèrent un nombre considérable,

et jusqu'à présent non rencontré, de cas de kystes pulmonaires (188). Parmi eux, 96 étaient atteints de volumineux kystes isolés (pour la plupart de nature echinococcique). 92 de ces malades étaient porteurs de multiples kystes congénitaux, occupant un ou plusieurs lobes. Les auteurs décrivent l'aspect clinique et radiologique de l'affection et en discutent l'origine congénitale.

Le diagnostic différentiel entre cette affection et les kystes bronchiectasiques se base sur les manifestations cliniques et radiologiques, qui correspondent aux constatations histopathologiques publiées dans la littérature. Les auteurs insistent sur l'importance de déterminer avec précision les différentes variétés de kystes pulmonaires. Il est rare que l'affection soit accompagnée de symptômes. Des manifestations cliniques peuvent apparaître lorsqu'elle se complique d'une infection secondaire.

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## Experiences with Tetraethyl Ammonium Chloride in Bronchial Asthma\*

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Since the introduction of tetraethyl ammonium as a ganglionic blocking agent, it has been used in the experimental induction of postural hypotension,<sup>1</sup> as a diagnostic aid in pheochromocytoma,<sup>2</sup> and, tentatively, in bronchial asthma and left ventricular failure.<sup>3,4</sup> Not only is the arterial blood pressure lowered, but the venous,<sup>5</sup> the pulmonary arterial,<sup>6</sup> and the pulmonary "capillary bed"<sup>7</sup> pressures are decreased as well. The cardiac output remains constant in human,<sup>8</sup> or falls in animal,<sup>9</sup> experiments. Tetraethyl ammonium compounds probably evoke epinephrine and norepinephrine hypersecretion.<sup>2,10</sup> These effects of the drug, as well as its autonomic blockade, should influence various cardiopulmonary derangements. The asthmatic state is definitely affected, as shown in the following study.

### *Methods and Materials*

Twenty patients with bronchial asthma were studied. They were given at various times tetraethyl ammonium chloride (Etamon§), 7 mg./kg. intravenously, epinephrine, 0.2 to 0.6 mg. intramuscularly, or aminophylline, 0.24 to 0.48 mg. intravenously. The vital capacity was determined in triplicate before administering the drug and at 30 to 60 second intervals immediately thereafter for five minutes, then less frequently up to the observed duration of effect. Previous experience indicated that serial vital capacity measurements were much more easily made and, in conjunction with the respiratory rate, as accurately reflective of the pulmonary function as the maximum breathing capacity.<sup>11</sup>

In many instances the patient was in *status asthmaticus* and unresponsive to the usual measures. Hence, some readings were obtained with two or more different drugs in succession. During these periods of remission a mild attack was induced with histamine in three cases, and Etamon and epinephrine then used as in spontaneous asthmatic attacks. Intravenous isotonic saline solution control readings were obtained in 11 cases.

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§Supplied by Parke Davis and Company.

### Results

The results are summarized in Table I. Significant rises (25 per cent or more) in vital capacity followed intravenous Etamon administration in 16 instances. In 19 other attempts, however, the vital capacity was unchanged (i.e., 13 cases) or fell 25 per cent or more (6 cases). Those patients responding favorably to Etamon showed drops in respiratory rate, pulse rate, and often marked diminution in dyspnea, cyanosis, apprehension, and signs of bronchospasm—within 60 to 120 seconds. Mild asthmatic attacks generally subsided rapidly, as is seen following epinephrine.

One severe case of status asthmaticus in a 58 year old woman in coma and in extremis, and refractory to epinephrine, aminophylline and oxygen, responded dramatically to 0.2 gm. of intravenous Etamon. The attack subsided and there was no recurrence up to 24 months. Of five patients refractory to epinephrine, two received Etamon with relief, whereas it had no effect upon the three other cases. Two persons refractory to amino-

TABLE I

Effects of Tetraethyl Ammonium, Epinephrine, and Aminophylline Upon the Vital Capacity of 20 Patients with Bronchial Asthma. A Rise was Defined as 25 Per cent or Greater Increase, a Fall as 25 Per cent or Greater Decrease, in Vital Capacity. Saline Injections (not shown, same criteria) Produced no Change in 10 Cases and a Fall in One Instance.

Etamon (7 mg./kg. I.V.)			
Vital Capacity	Rose	Same	Fell
Alone	12	9	4
After Epinephrine	2	3	0
After Aminophylline	0	1	1
After Histamine	2	0	1
<b>TOTAL</b>	<b>16</b>	<b>13</b>	<b>6</b>
Epinephrine (0.2-0.6 mg. I.M.)			
Vital Capacity	Rose	Same	Fell
Alone	6	1	0
After Etamon	10	2	0
After Aminophylline	2	0	0
After Histamine	1	0	0
<b>TOTAL</b>	<b>19</b>	<b>3</b>	<b>0</b>
Aminophylline (0.24-0.48 gm. I.V.)			
Vital Capacity	Rose	Same	Fell
Alone	3	1	0
After Etamon	6	1	0
After Etamon and Epinephrine	2	0	0
<b>TOTAL</b>	<b>11</b>	<b>2</b>	<b>0</b>

phylline failed to respond to Etamon. In histamine-induced asthma, Etamon was successful in two and unsuccessful in one instance.

Patients responding unfavorably to Etamon had continued symptoms and signs. The fall in vital capacity in six instances was accompanied by increased apprehension and dyspnea. No precordial pain was noted. The hypotensive effect of Etamon occurred equally in the favorable and unfavorable groups of cases.

Epinephrine, in contrast to Etamon, showed no unfavorable effects. In spontaneous, and, in one instance, in a histamine-induced attack, it caused a rise in the vital capacity of at least 25 to 50 per cent, or else no change (refractory asthma). In most instances the attack was consequently terminated within 60 to 120 seconds. Intravenous aminophylline had similar good results (Table I). Intravenous isotonic saline solution had no significant effect. The vital capacity never fell more than 25 per cent following epinephrine, aminophylline, or isotonic saline solution injections.

The following case reports elucidate the results obtained.

**Case 1:** J.M., a 14 year old colored male, had repeated moderate attacks of bronchial asthma. The vital capacity usually fell from about 3.0 liters between attacks, to 1.0-1.4 liters during the bouts of asthma. Figure 1 indicates that Etamon raised the vital capacity not more than 30 per cent in severe asthmatic bouts (IIc, III), and that epinephrine (III) and aminophylline (IV) were no more successful. In less severe asthma, however, both spontaneous and histamine-induced, the Etamon vital capacity ceilings rose both relatively and absolutely (IIa, IIb, V). In this case, Etamon consistently proved to be the best therapeutic measure. Control saline injections were ineffective (I).

**Case 2:** E.M., a 20 year old colored female, constantly affected by mild asthma (vital capacity 1.8 to 2.8 liters), occasionally very severe (vital capacity 0.2 to 0.4 liters). Figure 2 indicates the equivalent success of Etamon, aminophylline and

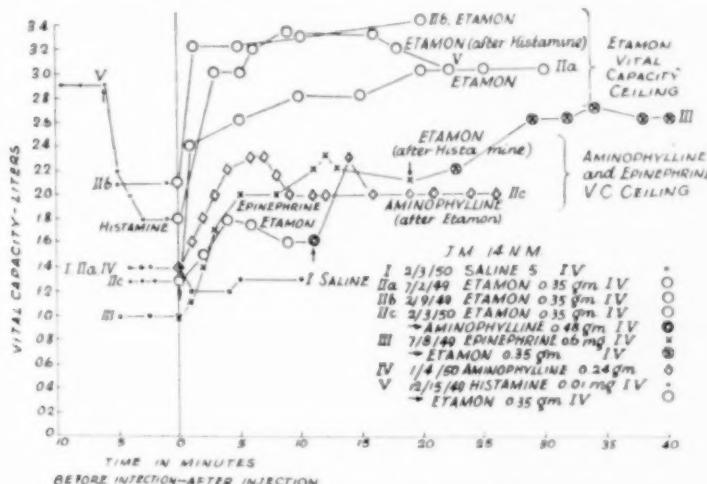


FIGURE 1: Effect of various drugs, alone and in combination, upon the vital capacity in patient J.M.

epinephrine in the mild attacks and their failure in the severe bouts of asthma. One moderate attack was unaffected by Etamon, then relieved by aminophylline (IIb). In another, an unusual diphasic effect of Etamon, a fall, then a rise in the vital capacity, was noted (IIa). Saline had no effect (Ia).

**Case 3:** M.B., a 49 year old colored male, with mild asthma. Severe attacks were induced by histamine (0.01 mg. intravenously), and then the therapeutic drugs injected. In this case (Figure 3), epinephrine (III, V, VI) and aminophylline were consistently superior to Etamon in raising the vital capacity and relieving the bronchospasm. Saline had no effect (Ia).



FIGURE 2: Effect of various drugs, alone and in combination, upon the vital capacity in patient E.M.

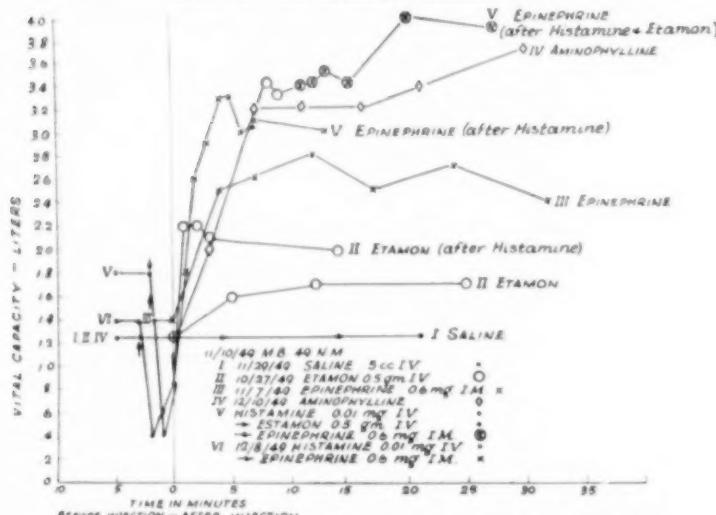


FIGURE 3: Effect of various drugs, alone and in combination, upon the vital capacity in patient M.B.

**Case 4:** W.F., a 44 year old white female with severe atopic bronchial asthma. Figure 4 indicates the failure of all drugs during severe status asthmaticus and the unfavorable effects of Etamon both in spontaneous (II) and histamine-induced (V) asthma. In milder asthmatic attacks aminophylline or epinephrine raised the vital capacity to approximately the same ceiling values. Following Etamon, epinephrine had strikingly beneficial effects (II, V). In this patient, as in other cases, too, the asthma was frequently refractory to epinephrine or aminophylline alone. However, after Etamon was administered, relief would be afforded.

To determine whether Etamon acted in part through release of epinephrine from the adrenal medulla, intramuscular epinephrine (0.003 mg./kg.) and intravenous Etamon (7 mg./kg.) were compared in their effects upon the four-hour afternoon eosinophil count<sup>12</sup> and the urine uric acid/creatinine ratio in nine patients, and upon the serum potassium (and sodium) levels in seven and eight patients respectively. (The subjects utilized were convalescent cases on the medical wards and free from allergic or endocrine disorders.)

Table II summarizes the eosinophil and the uric acid/creatinine ratio effects, and Figure 5 the serum potassium (and sodium) alterations of epinephrine and Etamon. Only four of the nine subjects, J.McN., B.D., C.P., and G.M., showed a significant fall in eosinophils four hours following both Etamon and epinephrine. A marked rise in the uric acid/creatinine ratios was seen only in case C.P. The potassium effects were grossly similar in that both Etamon and epinephrine caused rapid slight lowering of serum potassium in eight subjects each. Immediate falls in serum potassium following epinephrine in man have been reported previously.<sup>13</sup> The corresponding serum sodium alterations were inconclusively variable.

#### Discussion

It is clear that intravenous Etamon, in contrast to saline solution, has marked effects on bronchospasm. The latter, especially if not severe, is often dramatically relieved, even in cases refractory to epinephrine or aminophylline. However, there are cases and occasions in which Etamon has no effect, or the bronchospasm is actually augmented. Theoretically,

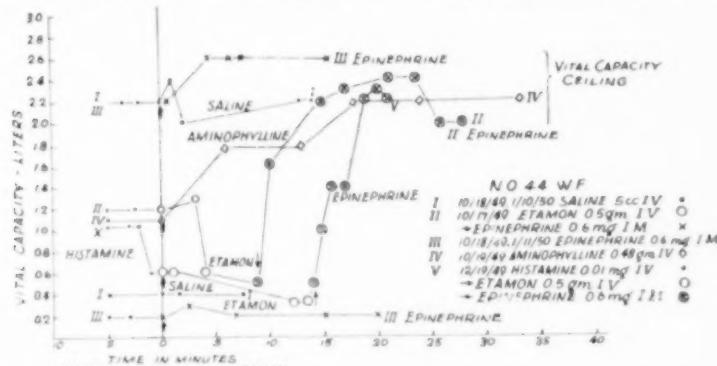


FIGURE 4: Effect of various drugs, alone and in combination, upon the vital capacity in patient W.F.

if the bronchial obstruction were primarily due to vagotonic bronchospasm, and if Etamon were to block primarily the vagal ganglia, the effect would be favorable, and if these conditions were not present—unfavorable. In this connection, another ganglionic blocking, and anticholinergic, agent—Banthine,\* was found in preliminary trials to raise the vital capacity favorably in some patients with bronchial asthma.<sup>14</sup>

\*G. D. Searle & Company brand of methantheline bromide.

TABLE II

Effect of Epinephrine (intramuscular, 0.003 mg./kg.) and Tetraethyl-ammonium (intravenous, 7 mg./kg.) Upon the Eosinophil Count and the Urinary Uric Acid/Creatinine Ratio (percentage change) in Normal Subjects Four Hours After Injection of the Drugs.

Subjects	EOSINOPHILS		URIC ACID/CREATININE	
	Epinephrine	Tea	Epinephrine	Tea
A.F.	-53	-5	-15	+18
J.M.	-18	-13	-10	-17
B.D.	-22	-55	+ 3	- 3
C.P.	-70	-22	+28	+43
G.M.	-48	-32	- 3	+ 2
C.B.	-60	- 7	-26	+10
N.T.	-70	+11	-14	- 8
H.F.	-67	+10	+28	+10
F.H.	-47	- 7	+34	+10

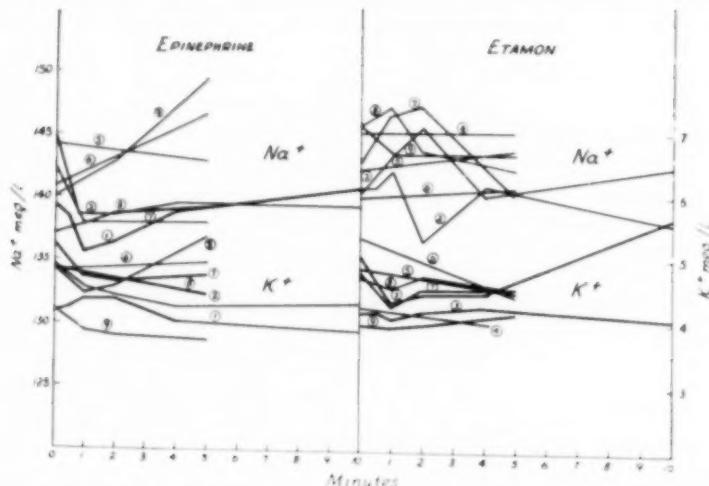


FIGURE 5: Effect of intramuscular epinephrine (0.003 mg./kg.) and of intravenous Etamon (7 mg./kg.) upon the serum sodium and potassium of human subjects. Note immediate falls (of 5 to 10 per cent or more) in five of seven cases following epinephrine and in five of eight cases following Etamon in serum potassium.

It is possible that the effects of Etamon in patients with asthma, as occasionally seen in patients with emphysema and left ventricular failure with pulmonary congestion,<sup>3,4</sup> may be, in part, due to its hemodynamic actions. The fall in pulmonary vascular resistance may be beneficial. Epinephrine and its analogs are, however, classically remedial, although they raise both the pulmonary and the systemic arterial pressures.

On the other hand, the systemic hypotension due to Etamon has caused serious, even fatal, coronary insufficiency in individuals with heart disease. While our patients had no heart disease and developed no anginal pain following Etamon, there was severe aggravation of asthma in a few cases. Like others,<sup>15</sup> we unfortunately had one fatality within 30 minutes following 0.2 gm. of intravenous Etamon, and are acquainted with another which occurred in a severe asthmatic attack treated with 0.5 gm. of intramuscular Etamon two hours previously. The fall in arterial pressure in these two cases was excessive, and epinephrine was of no aid.\*

Despite some parallelisms in the effects of Etamon and epinephrine upon the eosinophil count, urinary uric acid/creatinine ratio, and serum potassium, our data do not definitely prove the concept<sup>10</sup> that Etamon produces epinephrine release. In some instances, epinephrine following Etamon relieved previously refractory status asthmaticus; in other cases it failed to do so. Whether sensitization to, or increased secretion of, endogenous epinephrine and/or nor-epinephrine occurs following Etamon remains, therefore, *sub judice*.

#### SUMMARY

1) In 20 cases of bronchial asthma the effects of parenteral Etamon were compared with those of epinephrine and aminophylline during mild, severe, and histamine-induced attacks.

2) Parenteral tetraethyl ammonium chloride usually altered the asthmatic state: relief was more frequent than aggravation. Occasional fatalities contraindicate the use of TEA in bronchial asthma as well as in coronary heart disease.

3) The effects of TEA in asthma may be linked to ganglionic blockade, decreased pulmonary vascular resistance and pressure, and epinephrine sensitization. Some favorable effects of Banthine may support the first mode of action. Indirect signs of the intermediation of endogenous hyper-epinephrinemia in TEA action are discussed.

#### RESUMEN

1) En 20 casos de asma bronquial los efectos del Etamón parenteral fueron comparados con los de la epinefrina y la aminofilina durante ataques moderados, o severos, o bien en los ataques provocados por la histamina.

2) En general el tetraetilamonio cambió el estado asmático: El alivio fué mas frecuente que la agravación. Las defunciones ocasionales contraindican el uso del TEA en asma bronquial así como en la afección coronaria.

3) Los efectos del TEA pueden estar en relación con un bloqueo gan-

\*Nor-epinephrine was not used.

glionar, con una resistencia vasculo pulmonar disminuida, y sensibilización a la epinefrina. Pueden apoyar el primer modo de actuar algunos efectos favorables de la Banthina. Se discuten los signos indirectos de la intervención de la hiper-epinefrinemia en la acción del TEA.

#### RESUME

1) L'auteur a comparé dans 20 cas les effets de l'action parentérale de "l'Etamon" (chlorure tétra-éthyl-ammonium) avec l'action obtenue par l'adrénaline et l'aminophylline au cours de crises d'asthme moyennes, sévères, ou provoquées par l'histamine.

2) Le chlorure de tétra-éthyl-ammonium modifie en général l'état asthmatique. L'amélioration fut plus fréquente que l'aggravation. Des accidents peuvent contra-indiquer l'utilisation du tétra-éthyl-ammonium dans l'asthme bronchique, aussi bien que dans les affections coronariennes.

3) L'action du tétra-éthyl-ammonium dans l'asthme peut être lié au blocage des ganglions nerveux, à une diminution de la résistance et de la pression du système vasculaire pulmonaire et à une sensibilisation des surrénales. Les effets favorables de la "Banthine" peuvent apporter une confirmation au premier de ces mécanismes. L'auteur discute les manifestations indirectes d'un relais surrénalien au cours de l'action du tétra-éthyl-ammonium.

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## Experiences with Planography\*

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Planography, or as it is also called tomography, laminagraphy, stratigraphy or body-section radiography is today widely used in diagnostic radiology. It is of special value for an exact diagnosis of pathological changes in the lungs, but it can be used also for the examination of other organs.

The principle of this method, its technique and indications have been well described in the literature of the last 20 years.<sup>1-6</sup> This paper is a report on our experiences with planography of the chest during the last two years.

We are using an about 10 year old General Electric table with attachment for planography. It was originally constructed and used for the examination of the patient in horizontal position, but for the last two years we have been using it in the vertical position. Only for small children and patients who are too sick to sit upright we are using the table in the horizontal position. In our opinion the vertical position has definite advantages for examinations of the chest. These are firstly the same reasons for which we take plain x-ray films of the chest in this position, namely, the difference in the position of the heart and mediastinum which change due to gravity, the alteration in the position of the diaphragm and the difference in the respiratory expansion of the lungs. Secondly, fluid levels if present are visualized in the vertical but not in the horizontal position. Thirdly, we noticed that the table top is bending, especially under heavier patients, and by this the even movement of the Bucky diaphragm is hampered.

To check the accuracy of our equipment we are using lead numbers mounted in 1 cm. distances in a step like formation on balsa wood. This model<sup>1</sup> is fixed to the table so, that the numbers indicate their distance from the table top. Planograms of this model show only one of the numbers sharply outlined, the others blurred out (Figure 1). Using two such models, one placed centrally, the other near the margin of the cassette, it can be shown that the number of the latter one are somewhat less sharply outlined.

In order to obtain the best possible results we think it is important to place the patient so the central ray is directed towards the center of the lesion to be examined. Our standard technique is the following: The patient is first fluoroscoped and the center of the suspected lesion is marked with a skin pencil on the patient's chest. He is then placed with his back against the table so that the central ray is directed towards the marked spot. A scout film is now taken with the tube fixed in the horizontal position and one planogram in the layer the lesion is suspected. These two films are developed before further planograms are taken in order to check the exact

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<sup>1</sup>Model supplied by the Picker X-ray Corporation of Canada.

position of the patient and the exposure technique. The scout film is also helpful in identifying shadows on the planograms as it is taken at the same distance and with the patient in the identical position, whereas straight x-ray films and planograms differ in these two factors. For taking the planograms, the tube is put in the lower position and moved upwards by hand (Figure 2). As our exposure switch is not synchronized with the tube movement, the quality of the films depends to a large extent upon the skill of the technician. We are using a focus film distance of 36 inches and an exposure time of one second at 75 mA with a 2 mm. aluminum filter. This applies for the average size patient in A-P position. For lateral planograms we are using 100 to 150 mA seconds. Six to nine exposures in 1 cm. distances, usually on 8 x 10 films, are in most cases sufficient for a complete examination. On re-examinations often less films are needed.

Planography is indicated in all cases in which we want to obtain a more detailed analysis of pathological changes in the lungs, demonstrated on straight x-ray films. It is seldom that we find on planograms a lesion which we did not see or at least did not suspect from a plain film, taken in one of the standard positions (P-A, lateral, lordotic). But we are often surprised at the extent and qualitative appearance of the lesion on our planograms.

The diagnosis of a cavity in pulmonary tuberculosis is of extreme importance for the treatment and further prognosis of the disease. Among the various techniques described for the better roentgenological visualization of cavities planography gives by far the best results (Figure 3). Besides

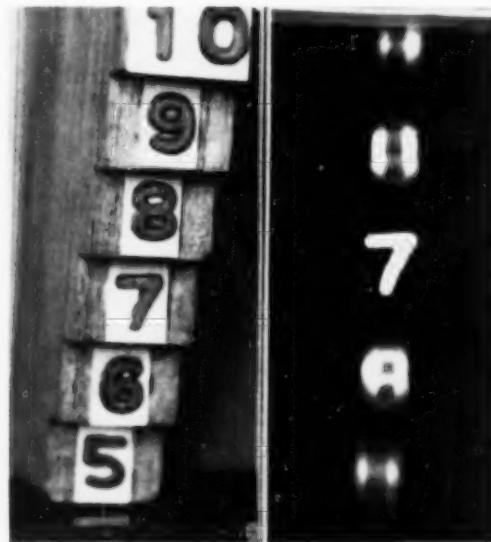


FIGURE 1A

FIGURE 1B

*Figure 1A:* Lead numbers mounted in 1 cm. distances on balsawood.  
*Figure 1B:* Planogram of this model in 7 cm. distance from table top.

demonstrating their presence, planograms show also their exact location, the condition of the cavity wall and surrounding lung tissue and often the draining bronchus. Furthermore, planographic re-examination in three to six monthly intervals is of invaluable help in checking the results of our treatment, the primary aim of which is the closure of cavities. On such re-examinations sometimes residual cavities can be demonstrated, undetectable on straight films (Figure 4). After thoracoplasties lateral planograms give often better results than those in A-P direction.

With the increasing use of lobar and segmental resections in the treatment of pulmonary tuberculosis, accurate localization of the lesions is most important. A-P and lateral planograms will be of great help to the surgeon for planning the operation.

Planography also proved extremely helpful for an exact analysis of minimal pulmonary lesions. As these are commonly located in the apices, they are, on straight films, hidden partly or completely behind the shadows of the ribs and of the clavicle. These apical lesions, often designated as obsolete foci or scars, have gained in importance since it has been recognized that they may form the starting point for progressive pulmonary tuberculosis (Initial foci by Hedvall<sup>7</sup>). It is therefore necessary to obtain a most accurate picture of these lesions in order to determine the need and type of treatment. Planograms enable us, better than any other method of examination to recognize details, as for example minimal cavities and thickened and tortuous bronchi. These pictures compare well with the pathological findings of Medlar<sup>8</sup> in his studies on the pathogenesis of tuberculosis. Repeated planographic examination of these cases will show earlier and in more detail, progressive or retrogressive changes in these

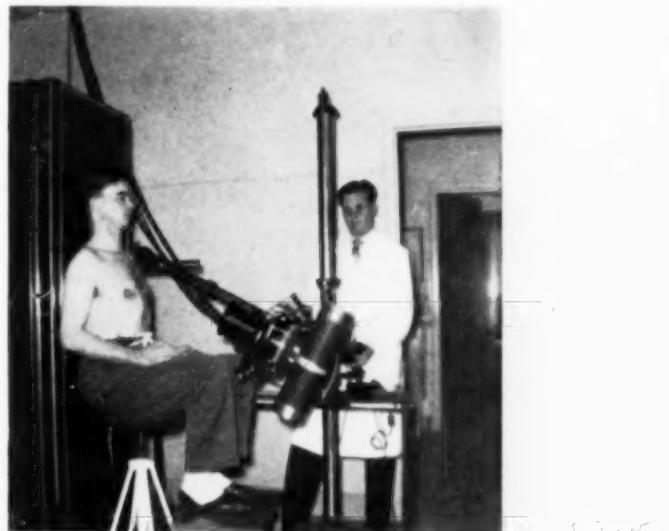


FIGURE 2: Patient in upright position for P-A planograms.

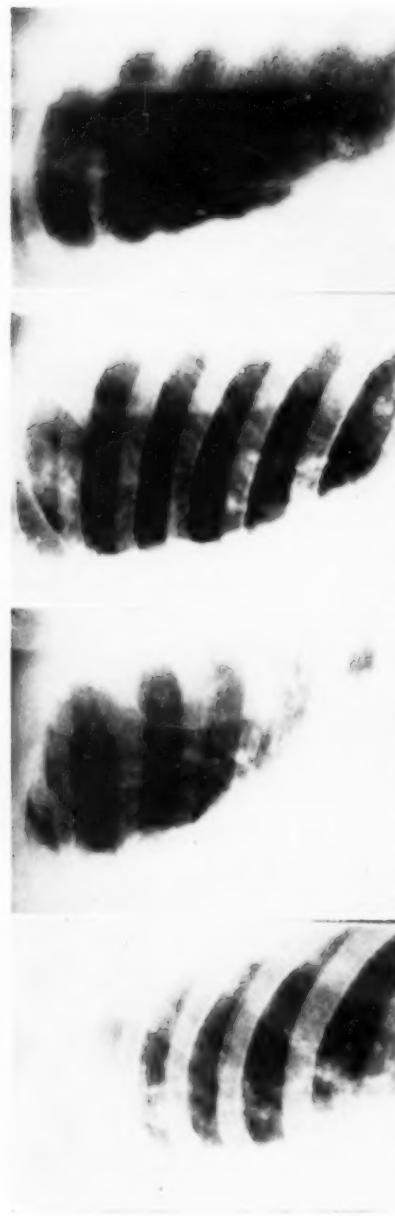


FIGURE 3A

*Figure 3A.* Patient C.T.: left upper lung field, straight P-A film.

*Figure 3B.* Same case, lordotic film. Shows no evidence of cavity.

*Figure 3C:* Same case, scout film taken in same position and distance as planograms. Suspect highlight in apex visible.

*Figure 3D.* Same case, planogram, 7 cm. level. Cavity clearly outlined.

FIGURE 3B

FIGURE 3D

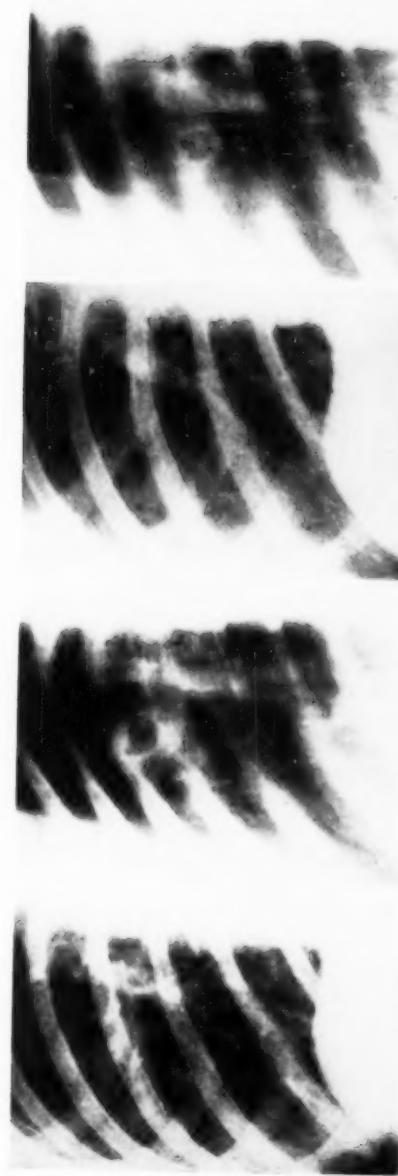


FIGURE 4A

FIGURE 4B

FIGURE 4C

FIGURE 4D

Figure 4A: Patient P.C.; right lower lung field, straight P-A film on admission to hospital.  
Figure 4B: Same case, planogram on admission, shows irregular outlined, thick walled cavity.  
Figure 4C: Same case, P-A film after four months' treatment with Streptomycin and PAS, shows considerable clearing and no evidence of the cavity.  
Figure 4D: Same case, planogram taken at the same time as Figure 4C, shows the cavity still present.

lesions and will therefore be a valuable guide in the management of these cases.

The interpretation of planograms is not always easy and requires experience. As in normal radiography of the lungs, no diagnosis of the activity of a lesion should be made from a single set of planograms alone. Serial planographic examination, however, or planographic findings correlated with bacteriological findings, may enable us to make a diagnosis of activity earlier and safer than it would be possible from straight x-ray films.

#### SUMMARY

The technique of planography of the chest as used at the Fort William Sanatorium in cases of pulmonary tuberculosis has been described. In most cases the patients are examined in the vertical position, placed so that the central ray is directed towards the center of the lesion. As in plain radiography of the chest, serial re-examination with planography seems to us most important. This will help in the evaluation of the effectiveness of our treatment and in the early recognition of progressive or retrogressive changes even in minimal lesions. The main indications for the use of planography in pulmonary tuberculosis are: the demonstration of cavities, the exact location of lesions prior to surgery, the detailed analysis of minimal lesions, especially in the apices.

Planography is used in addition to all other methods of examination which are necessary to make the diagnosis of disease as complete and accurate as possible.

*Acknowledgment:* I wish to thank Mr. U. Peuramaki, x-ray technician at the Fort William Sanatorium, for his excellent work in taking the planograms.

#### RESUMEN

Se ha descrito la técnica de la planografía del torax tal como se usa en el Sanatorio Fort Williams. En la mayoría de los casos los enfermos son examinados en la posición vertical colocados de manera que el rayo central se dirija hacia el centro de la lesión. Así como en radiografía simple, el examen en serie del torax por planografía nos parece muy importante. Esto ayudará a valorizar el resultado del tratamiento, y al reconocimiento temprano de cambios progresivos o regresivos aun en lesiones mínimas. Las indicaciones más importantes para la planografía en tuberculosis pulmonar son: demostración de cavernas, localización exacta de lesiones antes de la cirugía, análisis detallado de lesiones mínimas, especialmente en los vértices.

La planografía (tomografía) se usa además de todos los otros métodos de examen que son necesarios para hacer el diagnóstico de la enfermedad tan completo y exacto como es posible.

#### RESUME

L'auteur a déjà décrit la technique de tomographie des poumons, qui est utilisée au Sanatorium de Fort William pour la tuberculose pulmonaire. Dans la plupart des cas, les malades sont examinés en position verticale, et de telle sorte que le rayon central passe par le milieu de la lésion. De

même que lorsqu'il s'agit de cliché standard, il paraît extrêmement important à l'auteur de faire des examens tomographiques itératifs en série. Cette méthode sera d'un très grand secours dans l'évaluation de l'efficacité du traitement et dans la connaissance précoce des modifications progressives ou régressives, même dans les lésions minimes. Les principales indications de la tomographie en tuberculose pulmonaire sont la mise en évidence des cavités, la localisation précise des lésions avant l'acte chirurgical, l'analyse détaillée des lésions minimes, et plus spécialement celles du sommet.

La tomographie est utilisée en complément de toutes les autres méthodes nécessaires à un diagnostic aussi complet et rapide que possible.

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## Anterior Mediastinal Chondromyxosarcoma

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Anterior mediastinal chondromyxosarcoma is an extremely rare tumor. Since the prognosis in an individual case depends on early diagnosis and prompt institution of treatment, it is imperative that the findings both in rare and more common tumefactions become more known. The advances in thoracic surgery and roentgen therapy may offer the patients with malignant thoracic disease some ray of hope.

In an attempt to find similar cases, the literature in the English language was reviewed from 1930 to the present date. Several excellent reviews of thoracic and intrathoracic new growths were encountered. It was immediately apparent that the case to be presented was extremely rare. The sarcomas described by Harrington<sup>1</sup> apparently arose from the thoracic cage. In 1935, Harrington<sup>2</sup> discussed anterior and posterior mediastinal tumors, but made no mention of chondrosarcoma or chondromyxosarcoma. Harper<sup>3</sup> reported a case of chondrosarcoma which he believed arose from a benign chondroma. In Blades' review<sup>4</sup> of mediastinal tumors, he mentioned an osteochondroma of the mediastinum. Weisel and Ross<sup>5</sup> reported a chondrosarcoma of the posterior mediastinum with invasion of the lungs, ribs, and thoracic vertebrae. Lowell and Tuhy<sup>6</sup> reported a case of primary chondrosarcoma of the lung that closely resembled the case herein reported. It is stated that their case is the second case in medical literature.<sup>7</sup> Hence, this report is the third case of chondromyxosarcoma of the mediastinum.

The pathogenesis of this type of tumor in the mediastinum remains obscure. The presence of an embryonic rest may be postulated. However, the following explanation is probably more correct. Fibrous tissue, mucous tissue, and cartilaginous tissue are closely related. It is, therefore, possible to have the basic undifferentiated cell develop into any one or more of the tissues mentioned.<sup>8</sup>

**Case Report (abbreviated):** R.I., white, unmarried, 48 year old female, entered the hospital November 14, 1950, with the chief complaints of dyspnea and pain in the lumbar region.

The past history revealed treatment for pneumonia, while vacationing in Canada five months previously. Following return to the United States, she sought medical attention because of dyspnea and chest pain. Two roentgenograms of the chest were made, the second one week prior to admission to the hospital. Unfortunately, these films were not available, but were reported as normal.

One week prior to admission to the hospital, she suffered two bouts of hemoptysis (amounts not known). There was associated weight loss and night sweats.

The past history and family history were non-contributory.

**Physical Examination:** T. 101.8 degrees F., P. 80, R. 28, B.P. 120/80. The examination was essentially normal, except for a few scattered moist rales heard in the

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left infraclavicular region. During the examination, she had a paroxysm of coughing, resulting in hemoptysis.

The patient's course in the hospital was characterized by low grade fever, dyspnea, cough, and episodes of left chest pain resembling acute coronary occlusion. After six weeks in the hospital, the patient expired (Figures 1, 2, 3 and 4).

Blood chemistries, bacteriologic studies, and peripheral blood counts were within normal limits throughout the hospital stay. Tuberculin testing in all dilutions was negative. Electrocardiographic studies were consistent with a posterior wall infarction and/or acute pericarditis.

An abstract of the significant autopsy findings is as follows:

**A) Thorax:** The rib cage is removed in the usual manner. There are many dense white strands of tissue between the visceral and parietal layers of the pleura on all surfaces. Interspersed with these, there are many soft, easily broken, bands of white tissue. In attempting to open the pericardial cavity, the pericardium is found to be adherent to the heart. However, after stripping back the pericardium, the heart is found to be beneath a large mass which extends into the pericardial cavity. The lungs, heart, and trachea were removed en block. Further dissection revealed the mass



FIGURE 1



FIGURE 2



FIGURE 3

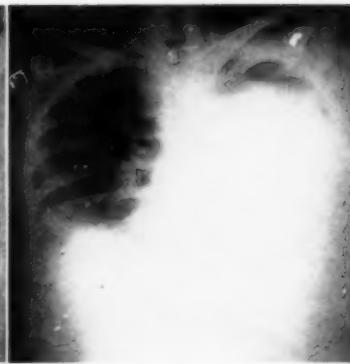


FIGURE 4

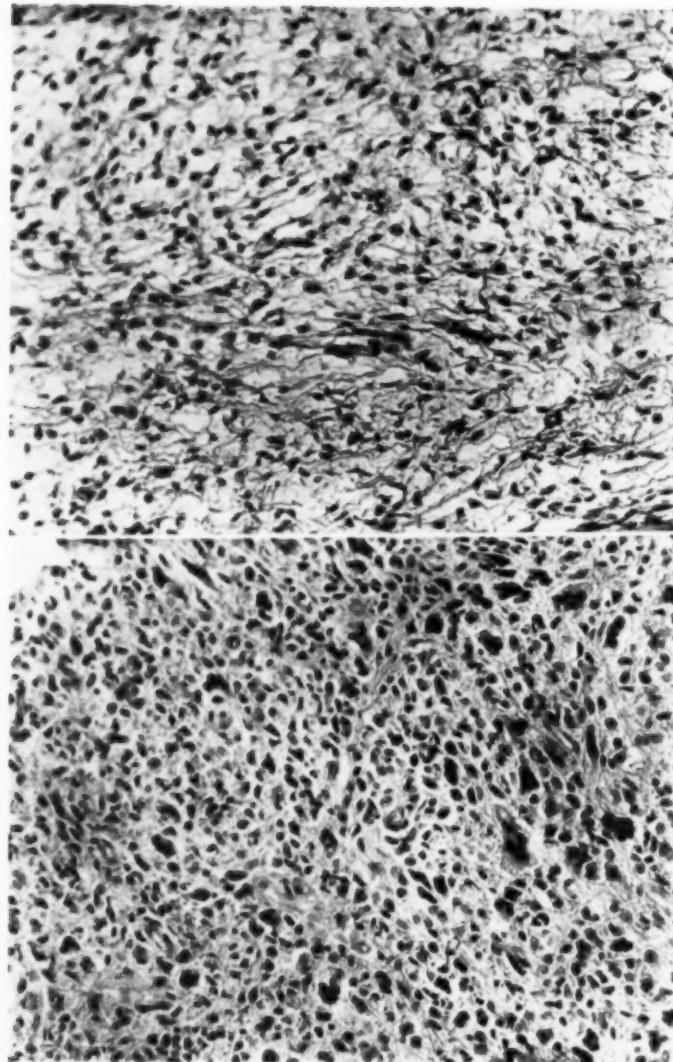


FIGURE 5: Demonstrates the chondrosarcomatous elements with primitive mesenchyme differentiating into myxomatous tissue. Many areas of extremely primitive development are noted. (200 X).

to be invading the pulmonary artery. There are several polypoid-like projections of a soft white tissue which is within the lumen of the vessel. The lumen of the pulmonary artery is seen to be partially filled by a solid plug of yellow white tissue which resembles fat, and is firmly adherent to the vessel wall. In many areas within the confines of the lung, branches of the pulmonary artery are seen to be plugged with a similar tissue which again is firmly adherent to the vessel wall.

**B) Lungs:** Portions of the left upper and left lower lobes are firm and non-aerated. In the left lower lobe there is a solid area which, on cut surface, is raised. This area is not aerated and is friable (Figure 5). The bronchi are patent throughout.

**C) Heart:** As previously mentioned the heart was covered by a mass of tissue measuring 15 cm. in diameter and 12 cm. in thickness. This mass was in part covered by pericardium.

No distant metastases were noted.

#### *Final Pathologic Diagnosis:*

- 1) Chondromyxosarcoma of the anterior mediastinum with growth into and along the pulmonary artery.
- 2) Infarct of the lung, left lower lobe, recent.
- 3) Pleural adhesions, bilateral, recent and old.

#### SUMMARY

A case report of an extremely rapidly growing chondromyxosarcoma of the anterior mediastinum is presented.

#### RESUMEN

Se relata un caso de un condromixosarcoma del mediastino anterior de extremadamente rápido crecimiento.

#### RESUME

Les auteurs présentent un cas de chondromyxosarcome du médiastin antérieur dont l'accroissement fut extrêmement rapide.

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## Byssinosis\*

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Inhalation of cotton dust over a long period of years may give rise to a disabling respiratory condition, and if cardiac failure supervenes, x-ray findings which are indistinguishable from advanced pulmonary tuberculosis. The infrequency of case reports in the American literature would indicate that either byssinosis is extremely rare in this country or the diagnosis is being missed. In England, where the working conditions in the cotton mills are said to be comparable to those in the United States, this disease has been extensively studied and its victims are eligible for compensation.

The name "Byssinosis" is derived from the Greek meaning "fine linen." Its existence has been known for over 100 years, but was first reported by Greenhow<sup>1</sup> in 1861. However, intensive investigative work was not done until the 1930's.

Trice,<sup>2</sup> investigating an outbreak involving some 25 to 30 workers reported that when the carding machines were cleaned with compressed air, a fog was produced which contained particulate matter and lint, and concluded that the exposure of the workers over a period of time to an excessive amount of the finer particles was responsible for the outbreak.

It had been previously suggested by Prausnitz<sup>3</sup> on the basis of animal experiments that the irritating soluble protein of the cotton dust penetrates into the alveolar tissue gradually producing thickening of the alveolar walls; simultaneously or perhaps even before, supersensitivity is acquired. Superficial irritation of the bronchial mucous membranes by the dust leads to chronic bronchitis, cough and ultimately emphysema.

Gill<sup>4</sup> divided the symptomatology into two periods. The early stage, a manifestation of sensitivity, consisting of a dry, irritative feeling in the throat and chest, is followed by a dry cough and sneezing. In a few cases urticaria and mild conjunctivitis may also be present. Within 24 hours all symptoms disappear. Usually there are no constitutional symptoms, although a few do have a low grade fever which is not incapacitating. Apparently most become immune in a few weeks or months, and it is usual for the workers to regard this as a "necessary baptism to the trade." These symptoms, occurring on entering the card room on Monday morning, have given rise to the terms "Mill Fever," "Monday Morning Fever," and "Factory Fever" by the workers. Rarely do these symptoms progress any further. In the late stage it is the stripper and grinder who succumb to the disease. Ten to 20 years following the initial attack, fever gradually reappears, the cough becomes dryer and more severe and the symptoms tend to occur every working day. Sputum is scant and apt to be tenacious and glairy. Easy fatigability is noted and work tolerance reduced. The slow progres-

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sion of symptoms continues and attacks of bronchitis become more frequent until finally the picture is one of far advanced pulmonary emphysema and fibrosis—continued cough, dyspnea, weakness and nocturnal attacks of breathlessness.

There are no distinctive physical signs in the early stage of the disease and those of the late stage are typical of emphysema. The patient looks chronically ill, poorly nourished, breathing is labored and cyanosis may be present. The chest is barrel-shaped, excursions are limited and the accessory muscles are called into play. The x-ray film is not diagnostic, but is usually consistent with emphysema and fibrosis. Pathologically, dilatation of the right heart and marked thickening of the alveolar walls are frequent. The diagnosis rests therefore on the history of long continued exposure to cotton dust with symptoms and the exclusion of other possible etiological factors.

#### Case Report

O. B., a 55 year old white veteran, was admitted to the Veterans Administration Hospital, Atlanta, Georgia, on December 12, 1949, complaining of intense dyspnea, cough and cyanosis which had been present intermittently for the preceding year, but had grown progressively worse. His history dated back to 1939, when, because of increasing shortness of breath and fatigability, he was forced to stop working as a framer and carder after 20 years in textile mills. In 1948 he was first hospitalized elsewhere for these symptoms and a diagnosis of pulmonary fibrosis and emphysema with myocardial insufficiency was made. He was placed on a salt-free diet, digitalized, given mercurial diuretics and bronchodilators and improved considerably. His chest x-ray film revealed extensive peribronchial and nodular infiltrations and the possibility of tuberculosis led to a determined search for the tubercle bacillus. Of some 14 specimens examined, one culture yielded a few colonies, and he was transferred to another hospital for the treatment of tuberculosis, where cultures of sputa and gastric washings were repeated and



FIGURE 1



FIGURE 2

*Figure 1: Roentgenogram (December 12, 1949) showing extensive peribronchial and nodular infiltrations.—Figure 2: Roentgenogram (January 23, 1950) showing reduction in heart size and some clearing of lesions peripherally.*

found negative. By that time he had sufficiently improved to return home, though on marked restriction of activity. For the ensuing months he had intermittent episodes of intense dyspnea and cyanosis, but he continued at home until December 12, 1949, when he was taken to a local hospital, and on the basis of chest x-ray inspection the diagnosis of tuberculosis was again made and he was referred to the Veterans Administration Hospital, Atlanta, Georgia. Physical examination on admission revealed an acutely ill, cyanotic and markedly dyspneic white male who was obviously malnourished. His neck veins were markedly distended. The chest was barrel-shaped with flaring of the lower ribs and widening of the intercostal spaces. Percussion note was hyperresonant. The breath sounds were obscured by numerous sibilant and subcrepitant rales heard throughout the entire chest. The heart borders could not be made out and the heart sounds were obscured by the noisy respirations. The rhythm was regular. Blood pressure was 95/50. There was definite cyanosis of the fingers and some curving of the nails though true clubbing was absent. X-ray inspection of the chest revealed (Figure 1) extensive peribronchial and nodular infiltrations located chiefly in the pericardiac regions of both lung fields and to a lesser extent peripherally. Hilar vascular markings were somewhat exaggerated. Red blood count was 3,900,000 with 11 grams of hemoglobin; white blood count was 6,650 with 63 per cent polymorphonuclears, 34 per cent lymphocytes and 3 per cent monocytes. Sedimentation rate was 38 mm./hr. Blood N.P.N. and chlorides were within normal limits. Repeated sputum cultures were negative. The hemagglutinin test was negative. The QRS complexes were of low voltage in all leads of the electrocardiogram, but the T waves were normal. He was placed on continuous oxygen, salt-free diet, digitalis and mercurial diuretics, and gradually improved (Figure 2). His sensorium was clouded on admission and a spinal tap was performed revealing clear fluid under normal pressure with normal sugar, protein and chlorides and absence of cells. By March 27, 1950 he was sufficiently improved to be discharged. At home he remained indoors, close to his bed and was moderately comfortable except for continued

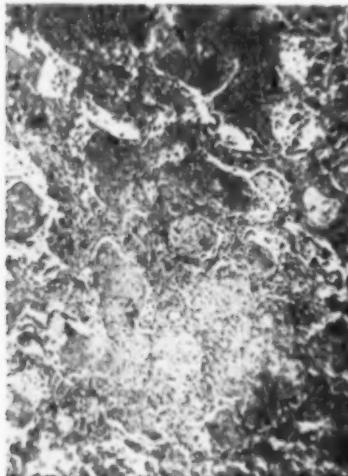


FIGURE 3

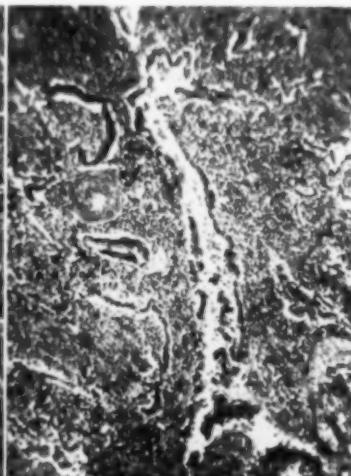


FIGURE 4

*Figure 3:* Photomicrograph of lung showing extensive fibrosis of alveolar walls; alveoli filled by hemorrhagic exudate.—*Figure 4:* Photomicrograph of lung showing lymphocytic infiltration of bronchial walls and interstitium; thickening of wall of bronchial artery.

attacks of nocturnal dyspnea. These gradually grew worse and on May 13, 1950 he was admitted to the Lawson Veterans Administration Hospital where he was found to be in marked cardiac failure. In spite of vigorous therapy he died nine days later.

Necropsy revealed the lungs to be voluminous. The right weighed 1,480 gm. and the left 1,050 gm. Crepitation was absent except for the apices in which large emphysematous blebs were present. Areas of firm consolidation were noted in all lobes. The cut surface was extremely moist and of a mottled yellow color, with rather extensive hemorrhagic areas seen. The bronchial orifices were slightly prominent and on dissection moderate ectasia was present with a sticky mucoid secretion adherent to the mucosal surface. The bronchial and hilar lymph nodes were enlarged. Microscopically (Figures 3 and 4) the pulmonary parenchyma exhibited markedly thickened and fibrotic alveolar walls with copious quantities of edema fluid and hemorrhage within the alveoli. Localized lymphocytic aggregates and hemosiderin deposits attested to the chronicity of the process. Epithelialization was prominent in areas of severe fibrosis. Foci of neutrophilic exudate were frequent and the bronchi and bronchioles showed varying degrees of ectatic change. One large blood vessel contained a big organized thrombus and there were numerous areas of patchy necrosis and neutrophilic reaction seen. The heart weighed 310 gm. The right ventricle and auricle were moderately prominent and there was marked enlargement and dilatation of both these chambers with the right ventricular wall measuring 1.3 cm. in thickness while the left measured 1.6 cm. The tricuspid valve measured 12 cm. and the pulmonary valve 8.5 cm., while the mitral was 10 cm. and the aortic 6.8 cm.

#### *Discussion*

The occurrence of respiratory symptoms in carders and strippers in the cotton industry has been known since 1818, but the recognition of the disease "Byssinosis" has been most difficult. Perhaps it is because the early symptoms are those of allergy and are not incapacitating. It is only after years of exposure to the dust that the affected worker becomes incapacitated and by then the clinical and pathological picture is one of advanced pulmonary emphysema and fibrosis. X-ray inspection is of little help in the diagnosis since findings resemble those of emphysema and may reveal evidence of right heart failure superimposed on it. In the case reported, the diagnosis of tuberculosis was made on the basis of the x-ray appearance and the findings of one positive sputum culture after innumerable negative smears, and the patient placed in a tuberculosis hospital. Necropsy failed to reveal any evidence of tuberculosis. Actually, the peribronchial and nodular lesions present in this case were secondary to hemosiderin deposits as a result of chronic congestive failure. Cotton dust has never been demonstrated in the lungs in chronic cases, but experimentally this has been demonstrated in animals. The characteristic pathological picture of marked thickening of the alveolar walls and the history of long exposure to cotton dust with severe, incapacitating symptoms makes the diagnosis of byssinosis most probable in this case. It should be stressed that the finding of a single positive sputum culture preceded or followed by numerous negative cultures must be carefully evaluated by the clinician and not accepted as absolute proof of tuberculosis. Though rare, errors can occur in the best laboratories where large numbers of specimens are handled.

It may be that in this country the paucity of reports may reflect better protection for the workers, though an acute episode involving some 25 to 30 individuals has been reported, or it is not thought of in the differential diagnosis and careful industrial histories are not being obtained. It is hoped that this report will serve to call the attention of the medical profession to the condition. With the improvement in methods for dust control in cotton factories and the use of safety measures, it seems likely to expect that this condition will be completely eradicated in the future.

#### SUMMARY

A case of "Byssinosis" is reported, and the infrequency of such reports in the American literature is stressed.

The history of the disease, its clinical manifestations and pathology are briefly reviewed. The diagnosis is dependent upon the taking of a careful industrial history. Terminally the x-ray appearance may simulate that of pulmonary tuberculosis.

#### RESUMEN

Se refiere un caso de "bisinosis" y se reclaca la escasa frecuencia de tales referencias en la literatura de los Estados Unidos de Norteamérica.

La historia de la enfermedad, sus manifestaciones clínicas, y su anatomía patológica se revisan brevemente. El diagnóstico depende de la historia clínica industrial cuidadosa. Al final la apariencia a los rayos X puede simular la de la tuberculosis pulmonar.

#### RESUME

L'auteur rapporte un cas de byssinose et insiste sur la rareté de telles observations dans la littérature américaine.

Il passe en revue rapidement l'histoire de la maladie, ses manifestations cliniques et son anatomie pathologique. Le diagnostic se base essentiellement sur l'étude attentive de l'activité professionnelle du patient. Enfin, l'aspect radiologique peut être tout à fait comparable à celui de la tuberculose pulmonaire.

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## Tuberculous Stenosis of the Trachea

Report of a Case Treated by Incision\*

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Severe stenosis of the trachea due to a fibrosing tuberculous tracheobronchitis is sufficiently unusual to warrant reporting a case which underwent marked clinical improvement following repeated incisions with a special knife designed for use through the broncho cope.

### *Introduction*

The incidence of tuberculous tracheobronchitis varies according to the index of suspicion of the investigators concerned. Naturally those who report statistics from autopsy material will find a greater occurrence of this condition than those who report bronchoscopic findings in living patients. It is generally accepted that autopsy material will reveal up to 70 per cent positive for tuberculous tracheobronchitis whereas bronchoscopically the figure varies from 15 to 20 per cent.<sup>1</sup> In our previously reported series,<sup>1</sup> 10 per cent of 100 cases of tracheobronchitis involved both the trachea and bronchi whereas only 3 per cent involved the trachea alone.

Sweaney and Behm<sup>2</sup> indicate "that Habershon in 1905 reported on 1,255 autopsies in which he found 10.4 per cent tracheal tuberculosis. Minkovsky in 1929 in a study of 2,379 autopsies found 11.48 per cent tracheal tuberculosis on gross examination. Bugher, Littig and Culp found 20.5 per cent tracheal tuberculosis in 122 cases studied both macroscopically and microscopically. Heafs reported 44 per cent tracheal tuberculosis in 133 autopsies." Sweaney and Behm themselves report that of 677 autopsy specimens, 377 were positive for tuberculous tracheobronchitis, 93 involving the trachea and bronchi and 31 (8.2 per cent), involving the trachea alone. This included only one case of stenosis of the trachea, the involvement being in its middle third.

Eloesser<sup>3</sup> in 1924 made the statement that while total obstruction of the trachea soon leads to death, the tracheal calibre may be astonishingly reduced without killing the patient. He reports two cases both with fatal outcome.

Of late there has been a trend to resect the stenosed portion of the trachea and reconstruct it with dermal grafts. The procedure is difficult and the mortality high. Gebauer<sup>4</sup> in 1950 reported four cases with 75 per cent immediate operative mortality. In 1951,<sup>5</sup> an additional case with good results was reported by the same author. Paulson,<sup>6</sup> in 1951, treated one tuberculous case by graft with good immediate result but the patient died on the way to the hospital a few weeks later because of suspected reactivation of submucosal tuberculosis in the left main bronchus.

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In view of the high operative mortality when surgical reconstruction was undertaken in humans by surgeons trained in such procedures by operating in many experimental animals, it was decided to treat the present case conservatively. The result to date, some 15 months later, is all we had expected and somewhat better than we had considered reasonable to anticipate.

#### Case Report

Mrs. H. D., age 31, was diagnosed as having moderately advanced tuberculosis and began treatment at home in April, 1947. A few weeks later she was admitted to St. Mary's Tuberculosis Unit pending transfer to the Nova Scotia Sanatorium on November 28, 1947. Sputum was repeatedly positive for tubercle bacilli.

When admitted to the Sanatorium, she was found to have a mixed exudative productive lesion apex to the fourth intercostal space on the right and throughout the entire left lung. No cavity was seen. Streptomycin was administered, 1.5 gm. per day, from December 6, 1947 to February 12, 1948, for a total of 105 grams. Marked clearing of the x-ray shadow casting lesion occurred. She gained 10 pounds and became symptom free except for a slight amount of expectoration which was negative for tubercle bacilli on culture. On April 20, 1948, she was discharged to continue treatment which she did faithfully under good home conditions. However, in August, 1949 her sputum became positive again but growth was inhibited by 1 microgram of streptomycin per cubic millimetre so her tubercle bacilli were considered to be still sensitive to the drug.

She was admitted to Point Edward Hospital, Sydney, N. S., on November 12, 1949, but was symptom free except for a small amount of positive sputum. Her blood sedimentation rate was 26 mm. (Westergren) and her x-ray film now showed evidence of extension of disease into the base of the left lung. Bronchoscopy did not reveal any evidence of tuberculous involvement of the trachea or bronchi and so a left phrenic nerve crush operation was performed. However, she began to run low grade fever and so pneumoperitoneum was induced on January 17, 1950, to augment the phrenic paralysis, but it was abandoned six weeks later as the sputum increased in quantity to approximately eight ounces daily. A bronchogram revealed some saccular bronchiectasis of the left lower lobe and so she was referred back to the Nova Scotia Sanatorium for consideration of major surgery.

On August 8, 1950, she was readmitted to the sanatorium with strength loss, some hoarsness of the voice, moderate cough, six ounces of sputum daily and fever of 99.6 to 100 degrees F. Sputum was positive for tubercle bacilli on direct smear. X-ray film revealed further extension of the disease within the left lung.

Bronchoscopy in August 18, 1950, revealed the presence of Type III<sup>1</sup> tuberculous tracheobronchitis involving the carina. The left main bronchus could not be visualized because of ulcerations and granulations on the left side of the lower end of the trachea and around the carina. Streptomycin was commenced, 1 gram daily, on August 24, 1950, and this was accompanied by PAS 5 grams daily until April 5, 1951, with the administration of a total of 225 grams of streptomycin and 1,600 grams of PAS at this time. From June 3 to August 31, 1951, she received another 90 grams of streptomycin and 450 grams of PAS. In addition, between September 25, 1950 and March 4, 1951, she received 30,662 mgm. of thiosemicarbazone.

Subsequent bronoscopies and their findings were as follows:

September 14, 1950: Granulation tissue increased but less generalized reaction. Granulations partly blocking the trachea, the lumen of which was now about one quarter its normal size. Treated with 30 per cent silver nitrate. She was receiving streptomycin and PAS.

September 30, 1950: Further stenosis of lower end of trachea. Lumen oval and reduced to about 4 x 2 mm. This was dilated and 30 per cent silver nitrate applied.

Bronchoscopist remarked, "Patient is in a very serious condition so should have oxygen immediately available." She was still getting streptomycin, PAS and thiosemicarbazone.

October 21, 1950: Less oedema noted and no granulations present. Lumen about the same size. Thirty per cent silver nitrate applied.

November 3, 1950: Lumen of trachea larger and left main bronchus seen for first time. Stenosis dilated and silver nitrate applied.

November 25, 1950: Further slight improvement noted.

December 15, 1950: Further slight improvement seen. Lumen slightly larger. However, x-ray film inspection after previous bronchoscopy revealed an asymptomatic massive atelectasis of left lung to have occurred.

January 12, 1951: Emergency bronchoscopy. Twenty minutes previously she suddenly became dyspnoic and cyanotic. Bronchoscopy revealed stenosis of the lower end of the trachea which would not admit the tip of a 3 mm. aspirator. Thickened secretion was blocking the stenosed lumen which was dilated and 30 per cent silver nitrate applied.

At this time surgical excision and reconstruction of the trachea was considered but thought to be unwise due to the precarious state of the patient, atelectasis of the left lung and the fact that the lesion involved the carina and the left main bronchus and possibly part of the right main bronchus.

January 26, 1951: Since previous emergency bronchoscopy she felt quite comfortable except for 10 minutes on January 11th when she suffered from marked dyspnoea which was relieved when she expectorated some thick sputum.

In preparation for this bronchoscopy, one of us (D.M. McR.) designed and had made a long stemmed cutting knife (Figure 1) for use through the bronchoscope. This was 50 cm. long and was made by hammering out and sharpening one end of a brass rod one eighth inch in diameter. Its cutting blade was rounded and could be advanced through the bronchoscope until it just protruded beyond the end of the tube which could then be used as a guard.

With this instrument incisions were made in the constricting ring at approximately one and four o'clock on its circumference so that a small triangular flap of tissue was released from the constricting ring. This piece of loose tissue was treated with 30 per cent silver nitrate.

February 9, 1951: Following previous incision of constricting ring, she showed marked clinical improvement with disappearance of wheezing and dyspnoea and more adequate drainage of secretions.

At bronchoscopy the lumen was estimated to be about 5 mm. in size. Another incision made at four o'clock on its circumference and the lumen dilated. Twenty five per cent silver nitrate applied.

February 23, 1951: Bronchoscopy revealed overall improvement but some further narrowing of the stenotic lumen had occurred.

May 12, 1951: All medication had been stopped early in April and she was feeling

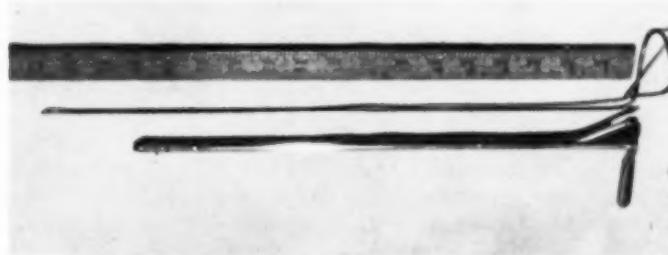


FIGURE 1

well. Examination revealed the stenotic lumen to have increased slightly in size. An attempt was made to enlarge it further by incising the ring on either side of its circumference at three and nine o'clock. This, apparently, was a tactical error as she developed increasing dyspnoea which progressed to almost complete asphyxia five hours later. An emergency bronchoscopy was again performed by one of the authors (F.J.M.) and two tags of scar tissue were seen to block almost completely the airway in the expiratory phase although the air passage was relatively clear on inspiration. Secretion was aspirated and then a small tissue tag removed by means of foreign body forceps. Almost instant relief was noted. Silver nitrate was applied.

October 6, 1951: She was feeling well. No wheezing. Bronchoscopy revealed lumen to be round in shape and 5 to 6 mm. in diameter. X-ray film now revealed considerable re-aeration of the lung.

April 5, 1952: She was feeling well. No wheezing experienced and rhonchi were not heard. Bronchoscopy revealed the stenosed area at the lower end of the trachea to be possibly slightly narrower than previously, the lumen being about 4 mm. in diameter.

April 13, 1952: She was discharged to her home for three months at her request with provision made for immediate readmission to the sanatorium should wheezing or dyspnoea recur. Her sputum had been negative for tubercle bacilli on culture (39 tests) since October, 1950.

#### SUMMARY

We have presented a case of tuberculous ulceration of the trachea (Type III) which progressed to marked stenosis (Type IV). Due to the high mortality rates quoted in the literature in regard to the surgical removal and repair of the lower end of the trachea it was decided to treat conservatively with massive antibiotic therapy combined with repeated local incisions of the constricting band. It is granted that the patient's future is still precarious but she has been kept alive for 15 months since the constrictive crisis, she is relatively well, her sputum has been converted and she has returned home to continue convalescence. The atelectasis of her left lung has lessened and her general condition is such that she could now stand excisional therapy for the trachea better than would have been the case when she was so ill in January 1951. The repeated incisions of the constricting tracheal ring were accomplished by a special instrument designed by one of the authors rather than by cautery as it was feared that the reaction to the latter might seriously increase the degree of stenosis.

#### RESUMEN

Hemos presentado un caso de ulceración de la tráquea (tipo III) que evolucionó hacia la estenosis progresiva (tipo IV). Debido a la elevada mortalidad referida en la literatura, sobre la extirpación y la reparación de la porción baja de la tráquea, se decidió por el tratamiento conservador con terapia masiva antibiótica combinada con incisiones locales reiteradas sobre la banda de constrictión. Se admite que el futuro de la enferma es aún precario pero se ha conservado viva por 15 meses desde la crisis constrictiva, se encuentra relativamente bien, el esputo se ha tornado negativo y ha vuelto a su hogar para continuar su convalecencia. La atelectasia del pulmón izquierdo ha disminuido y su estado general es tal que ahora puede

soportar el tratamiento de excisión de la traquea mejor que lo que hubiese podido cuando se encontraba tan enferma en Enero de 1951. Las incisiones reiteradas sobre el anillo constrictivo se llevaron a cabo con un instrumento especial ideado por uno de los autores en lugar de usar el cauterio porque se temió que la reacción a este último podría aumentar el grado de la estenosis.

#### RESUME

Les auteurs présentent un cas d'ulcération tuberculeuse de la trachée qui évolua progressivement jusqu'à une sténose intense. Etant donné la haute mortalité qui est liée à l'extirpation chirurgicale, et à la réfection de la partie inférieure de la trachée, ils décidèrent un traitement médical à l'aide d'antibiotiques à hautes doses. Ils combinèrent ce traitement avec des incisions locales répétées de la zone de striction. Les auteurs admettent que le pronostic reste encore très précaire, mais ils font remarquer que leur malade est encore en vie après 15 mois, que son état est relativement bon que les bacilles ont disparu de son expectoration et qu'elle est rentrée chez elle pour poursuivre sa convalescence. L'atélectasie de son poumon gauche a diminué et son état général est tel qu'elle pourrait actuellement subir un traitement chirurgical mieux que si on l'avait tenté au début de l'affection. Les incisions itératives de l'anneau de striction trachéale furent exécutées par un instrument spécial conçu par l'un des auteurs. Ils ont préféré cette technique que l'utilisation du cauther dont les réactions ultérieures auraient pu augmenter sérieusement l'importance de la sténose.

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## Audio-Visual Educational Methods in Cardio-Pulmonary Disease\*

J. SCOTT BUTTERWORTH, M.D.

New York University Postgraduate Medical School

The medical student of today must assimilate an almost unlimited and constantly changing mass of scientific facts in the same four years of study prescribed for his father. Part of this is due to the augmentation of the therapeutic armamentarium with the advent of chemotherapy and it has sorely strained the students' capacity of absorption.

To catalyse the powers of orderly assimilation of information and facts, it is obvious that thought must be given to educational curriculum and methodology. Some noteworthy attempts are being made by several institutions in curriculum integration and instructional aids and new methods are slowly being introduced. The fact remains, however, that improvement in these aspects can barely keep abreast of new advances in medicine. The frightening, engulfing shadows of rising mountains of useless medical literature is terrifying.

For the past several years the division of cardiology of the New York University Post-Graduate Medical School has been probing for methods to accelerate the learning processes. In general, we have proceeded along the line of developing apparatus and equipment, generally known as audio-visual aids. (The term, unfortunately, causes some of our more respected deans and professors to wince and suddenly become incomprehensible of even the simplest logic. This is perhaps wise and just since it would require little stimulus for audio-visual aids to multiply asexually as the square. Whereas we are now wading to our knees in journals we would be smothered by the compression of machines, models, instruments, gadgets, lights, and thing-a-majigs beyond description).

We have found, however, that as with every new movement there is some good with the bad and I am going to describe briefly a few pieces of equipment and methods which we have found useful under continued classroom experimentation.<sup>1</sup>

Perhaps our most useful tool is an electronic monster, known familiarly as "Cyclops,"<sup>2</sup> which uses an eye, a 16 inch television-type screen with a special coating to retain light so that the path of the electron beam will persist for several seconds before disappearing. On this tube can be electronically painted electrocardiograms, vectrocardiograms, ballistocardiograms, and stethograms so that a large group can easily follow the instantaneous changes in patterns. Combined with this is an electronic sound system which faithfully reproduces the sounds as heard through an ordinary stethoscope. For the reproduction of sounds which are transient and not

\*The third in a series of articles prepared under the sponsorship of the Council on Undergraduate Medical Education of the American College of Chest Physicians.

always easily available in patients (i.e. friction sounds) a special tape recorder is provided.

This equipment enables a large group of students (limited only by their ability to see the screen) to listen to sounds produced by the heart, lungs, or vascular system of the body and at the same time to look at the electrocardiogram or stethogram.

Briefly the advantages of this scheme, as observed in both undergraduate and postgraduate students, are: The 50-fold, or more, saving in time by group auscultation; The lack of conversational room noise because of the simultaneous group concentration; The "painless" examination of the patient; and the tremendous manpower saving since one instructor can easily replace several instructors.

We could mention several other devices which are in constant use, such as the fluorodemonstrator for teaching cardiac fluoroscopy, angiocardiography and vectrocardiography; and fluorescent chalks and paints activated by "black light" to enable the instructor to illustrate in the dark while showing slides. But these are simply the details of the program, important, but not necessary to be described here.

The essential requirement of audio-visual methods, as with any innovation in education, is that the methods accelerate and make more acute and permanent the learning processes. We feel that our attempts have been a great improvement but are merely stepping stones to this end.

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- 1 J. Scott Butterworth and Poindexter, Charles A.: "Visual and Auditory Educational Aids in Cardiology," *J. Med. Ed.*, 27:285, 1952.
- 2 Educational Electron Cardioscope, Cambridge Instrument Company.

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## Resident Fellowship Report

In June, 1951, with the approval of the Board of Regents of the College, the Committee on Resident Fellowships in Chest Diseases was established for the purpose of assisting qualified physicians throughout the world in receiving post-graduate training in the recent advances in the diagnosis and treatment of heart and lung diseases.

Immediately after the establishment of administrative procedures, the committee, with the aid of the Executive Offices of the College, undertook the task of corresponding with appropriate medical institutions in the United States which maintain chest clinics or hospitals and sanatoria established for the purpose of treating tuberculosis and allied disorders. The response was gratifying as many institutions offered interesting residencies, including full maintenance in addition to a small stipend. As soon as these institutions indicated their willingness to accept Resident Fellows, officials of the College throughout the world were notified of the available opportunities which existed for postgraduate training. The officials were supplied with appropriate application forms and within a very short period thereafter, the Committee on Resident Fellowships had the difficult task of screening the many applications that were received.

To facilitate the many problems encountered in obtaining visas, the American College of Chest Physicians applied for an Exchange Visitors Program number which was immediately approved by the Department of State.

During the past two years, the Committee on Resident Fellowships has approved 46 applications and from this number, 18 physicians have received fellowships in hospitals where they have or are now receiving training of their own choice within the specialty of heart and lung disease. At the present time, there are 15 physicians undergoing postgraduate training in the United States from the following countries: South Africa, England, Japan, India, Brazil, Spain, Panama, Nicaragua, Chile, Israel, Argentina, Formosa, Austria, Turkey, and Peru.

This program has been highly commended by the Pan-American Sanitary Bureau, the United States Department of State, and many other government and private organizations.

Physicians interested in receiving such postgraduate medical training in chest diseases are advised to write for appropriate application forms to the Executive Offices of the American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois, U.S.A.

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## College Chapter News

### **NORTH CAROLINA CHAPTER**

The North Carolina Chapter met on October 16 at the Veterans Administration Hospital, Oteen, for its afternoon session and the Battery Park Hotel, Asheville, for its evening session and banquet at which Dr. Otto C. Brantigan, Baltimore, Governor of the College for Maryland, was guest speaker on the subject "Mediastinal Tumors". The following were elected officers:

Ralph E. Moyer, Oteen, President  
E. S. Avery, Winston-Salem, Vice-President  
Norman L. Anderson, Asheville, Secretary-Treasurer (re-elected).

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### **NEW YORK CHAPTER**

The Clinical Meeting of the New York Chapter will be held at the Hotel New Yorker, New York City, February 18, 1954. Dr. Ida Levine, Brooklyn, is Chairman of the Program Committee for the meeting.

**KENTUCKY CHAPTER**

The annual meeting of the Kentucky Chapter was held at the Brown Hotel, Louisville, September 23. Guest speaker was Dr. Paul H. Holinger, Chicago, Illinois, whose subject was "Congenital Anomalies of the Bronchial Tree." Officers elected for 1953-1954 are:

John S. Harter, Louisville, President  
Lawrence A. Taucher, Louisville, Vice-President  
A. B. Muilen, Waverly Hills, Secretary-Treasurer.

**MICHIGAN CHAPTER**

The scientific meeting of the Michigan Chapter was held in conjunction with the meeting of the state medical society in Grand Rapids, September 23. Dr. Lawrence Pratt, President of the chapter, was moderator of the discussion on "The Modern Medical and Surgical Treatment of Pulmonary Tuberculosis," the theme of the chapter meeting. Dr. Paul Chapman led the discussion of the medical treatment and Dr. Richard Meade, the surgical treatment. Drs. William A. Hudson and Forest Dodrill summarized for the surgeons and Dr. Willard Boyden Howes summarized for the clinicians.

**WISCONSIN CHAPTER**

At the annual meeting of the Wisconsin Chapter, held at the Schroeder Hotel, Milwaukee, October 4, the following members were elected to office:

William Thaw Clark, Janesville, President  
Elston L. Belknap, Milwaukee, Vice-President  
Leon H. Hirsh, Milwaukee, Secretary-Treasurer (re-elected).

Approximately 200 physicians attended the scientific sessions. Guest speakers at the meeting were: Alvis E. Greer, Houston, Texas, President, American College of Chest Physicians; Edwin R. Levine, Kenneth C. Johnston, Albert H. Andrews, Jr., Ernest Teller, and Abel Froman, Chicago, Illinois; Alfred Goldman, Los Angeles, California; and Harold G. Trimble, Oakland, California.

**ROCKY MOUNTAIN CHAPTER**

New officers of the Rocky Mountain Chapter, elected at their annual meeting at the Shirley Savoy Hotel, Denver, Colorado, October 3 are:

John S. Bouslog, Denver, President  
Sidney H. Dressler, Denver, First Vice-President  
William F. Stone, Colorado Springs, Second Vice-President  
Leroy Elrick, Denver, Secretary-Treasurer.

**SOUTHERN CHAPTER**

The Southern Chapter, encompassing 16 states and the District of Columbia, met at the Henry Grady Hotel, Atlanta, Georgia, October 25-26, in conjunction with the meeting of the Southern Medical Association. Chapter officers elected for 1953-1954 are:

John S. Harter, Louisville, Kentucky, President  
George R. Hodell, Houston, Texas, First Vice-President  
Alfred Goldman, St. Louis, Missouri, Second Vice-President  
Joseph S. Cruise, Atlanta, Georgia, Secretary-Treasurer.

A resolution to establish the "Paul A. Turner" annual lecture was unanimously adopted at the meeting. Dr. Turner was Past-President of the Southern Chapter and Chairman of the Board of Regents of the College at the time of his death. The first lecture will be given at the annual meeting of the Southern Chapter in the fall of 1954.

**FINNISH CHAPTER ORGANIZED**

At a meeting in Helsinki on July 30, the Finnish Chapter of the College was organized. Dr. P. E. A. Nylander, Helsinki, Professor of Surgery at the University of Helsinki and Governor of the College for Finland, was elected President of the Chapter and Dr. Jorma Patiala, also of Helsinki, was elected secretary.



Left to right: Drs. K. Kivikanervo, E. Tiitinen, N. Turunen, R. Elo, O. Perasalo, Mr. Kornfeld, P. Haldnen, A. Stinford, J. Patiala, H. Laitinen and P. E. A. Nylander.

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**NORTHEAST BRAZIL CHAPTER**

On October 16, in Recife, the Northeast Brazil Chapter presented a symposium on "Present Status of Collapse Therapy in Pulmonary Tuberculosis," presided over by Dr. Joaquim Cavalcanti, Recife, Governor of the College for Pernambuco. The discussors were Drs. Agenor Bonfim, Ferreira Pinzon, Aldo Vilas Boas, and Angelo Rizzo. The chapter presented the following program on October 17 at the Hospital Oswaldo Cruz:

"Alveolar Cell Carcinoma,"  
Humberto de Menezes.

"Bronchography in Pulmonary Tuberculosis,"  
Jose Martins.

"Middle Lobe Syndrome,"  
Joaquim S. Cavalcanti.

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The following members of the College spoke before the Annual Meeting of the American Cancer Society, November 1-6, New York City: Drs. Arthur J. Vorwald, Alton Ochsner, Robert J. Anderson, Katharine Boucot, Richard H. Overholt, Leo G. Rigler, William F. Rienhoff, Jr., Evarts A. Graham and John L. Pool.

## ITALIAN CHAPTER



Dr. Charles A. Smolt, Ventura, California, spoke on "Present Use of Drugs and Antibiotics in Tuberculosis" before members of the Italian Chapter of the College at the Carlo Forlanini Institute, Rome, May 17. Dr. and Mrs. Smolt appear in the center of the above photograph and on Dr. Smolt's right is Professor Eugenio Morelli, Regent of the College for Italy. On Mrs. Smolt's left is Professor A. Omodei Zorini, Director of the Institute and Governor of the College for Northern Italy.

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### College News Notes

The following Fellows of the College attended the First World Congress on Medical Education, held in London, England, on August 23-29, 1953: Erik Carl E. F. Ask-Upmark, Uppsala, Sweden; Wilhelm Loeffler, Zurich, Switzerland; Raman Viswanathan, New Delhi, India; Helge Bertil Wulff, Malmo, Sweden. Mr. Murray Kornfeld, Executive Director of the College, also attended the congress. Over 600 medical educators, representing 92 medical schools and 59 countries attended the meeting.

Dr. J. J. Kirshner, Philadelphia, Pennsylvania, was elected Medical Director of the Eagleville Sanatorium, Philadelphia, by the sanatorium board.

Dr. Mario Pastor Balcazar, Lima, Peru, was elected President of the Peruvian Tuberculosis Society for 1953-1954 at a meeting held in Lima in October.

Dr. Harold Guyon Trimble, Oakland, California, Associate Clinical Professor of Medicine, Stanford University Medical School, presented a paper on "Emphysema, the Medical and Surgical Treatment" before the Societe Francaise De Pathologie Respiratoire on May 14 in Paris, France. Dr. Trimble was introduced by Dr. Etienne Bernard, Regent of the College for France, who presided at the meeting, and by Andre Meyer, Governor of the College for Paris.

## MEETING IN SWITZERLAND

Dr. Francis M. Woods, Governor of the College for Massachusetts, addressed a joint meeting of the Medical Society of Lausanne and the Climatological Society of Switzerland at Leysin, June 30. The meeting was arranged by Professor Maurice Gilbert of Geneva, Governor of the College for Switzerland, and was presided over by Dr. Gerard Favis, President of the Medical Society of Lausanne. More than 100 physicians attended the meeting. Dr. Woods presented the motion picture "Extra Periostal Lucite Ball Plombage for Pulmonary Tuberculosis" prepared by the Overholt Thoracic Clinic, Brookline, Massachusetts. Plans for the organization of a College chapter in Switzerland were discussed at the meeting which was also attended by Mr. Murray Kornfeld, Executive Director of the College.



Dr. Francis M. Woods (standing) addressing Medical Society of Lausanne and Climatological Society of Switzerland.

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Dr. Charles K. Petter, Waukegan, Illinois, Superintendent and Medical Director of the Lake County Tuberculosis Sanatorium and Treasurer of the College, was a guest speaker at the 75th Annual Meeting of the Montana State Medical Association on September 17 held in Billings. Dr. Petter's subject was "An Evaluation of the Newer Methods of Treatment of Tuberculosis."

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Dr. Harold A. Lyons has recently been appointed Associate Professor of Medicine at the State University College of Medicine, Brooklyn, New York.

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In the October 19 issue of *Newsweek Magazine*, there appears an article concerning the Columbia-Presbyterian Medical Center in New York City. Listed among the many famous research contributions of the center is that of the development of the first practical oxygen tent and the first use of helium-oxygen mixture for obstructed breathing by Dr. Alvan L. Barach, New York City, who presently is serving as Vice-Chairman of the Council on Research of the College.

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Gerald L. Crenshaw, M.D., Oakland  
Glenroy N. Pierce, M.D., San Francisco  
Donald F. Rowles, M.D., Oakland  
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## COLLEGE EVENTS

### NATIONAL AND INTERNATIONAL MEETINGS

**20th Annual Meeting, American College of Chest Physicians,**  
San Francisco, California, June 17-20, 1954.

**Third International Congress on Diseases of the Chest,**  
American College of Chest Physicians,  
Barcelona, Spain, October 4-8, 1954.

### CHAPTER MEETING

**Clinical Meeting, New York Chapter, Hotel New Yorker, New York City,**  
February 18, 1954.

## MEDICAL SERVICE BUREAU

### POSITION WANTED

*Husband and wife, both physicians, seek staff appointments in the United States in a tuberculosis sanatorium. Wife is graduate University of Michigan, trained at Bellevue Hospital Chest Service, age 38. Husband is graduate of University of Paris (France) age 42, presently medical director of a 300 bed sanatorium, experienced in bronchoscopy, thoracoscopy, and respiratory physiology. Husband and wife desire full maintenance and salary. Please address all inquiries to Box 281B, American College of Chest Physicians, 112 E. Chestnut St., Chicago 11, Illinois.*

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*The Veterans Administration Hospital, Kerrville, Texas, a 449 bed tuberculosis hospital, has vacancies for an assistant surgeon, a chest physician (general practitioners eligible) and a pathologist. Starting salaries up to \$10,800; positions based on the applicant's education and experience. Approved by American College of Surgeons and American Hospital Association, as well as possible residency training. Affiliated with diplomate consultants in the various specialties who make regular visits. In the hills of Southwest Texas, only 56 miles from San Antonio. Contact the Manager, Veterans Administration Hospital, Kerrville, Texas.*

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